Epidemiologic Study Designs

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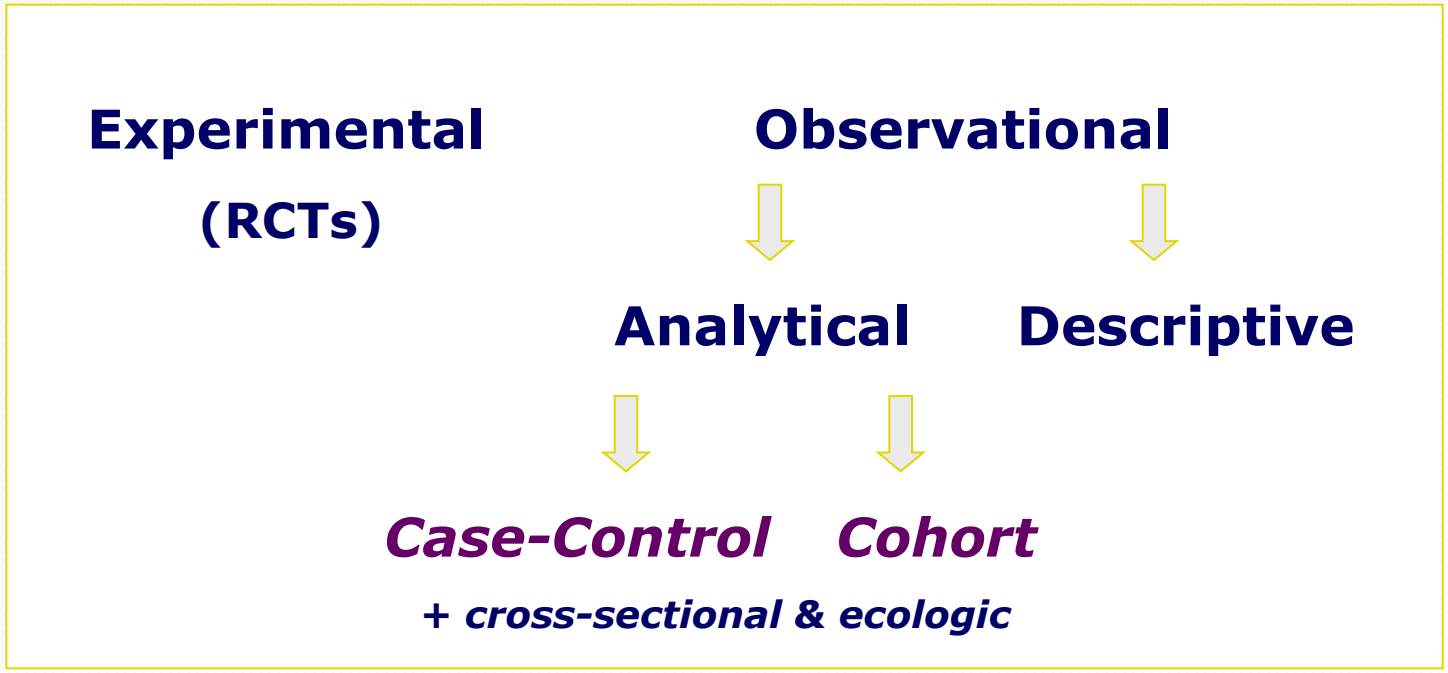
Epidemiologic Study Designs



Epidemiologic Study Designs

Descriptive studies

Examine patterns of disease

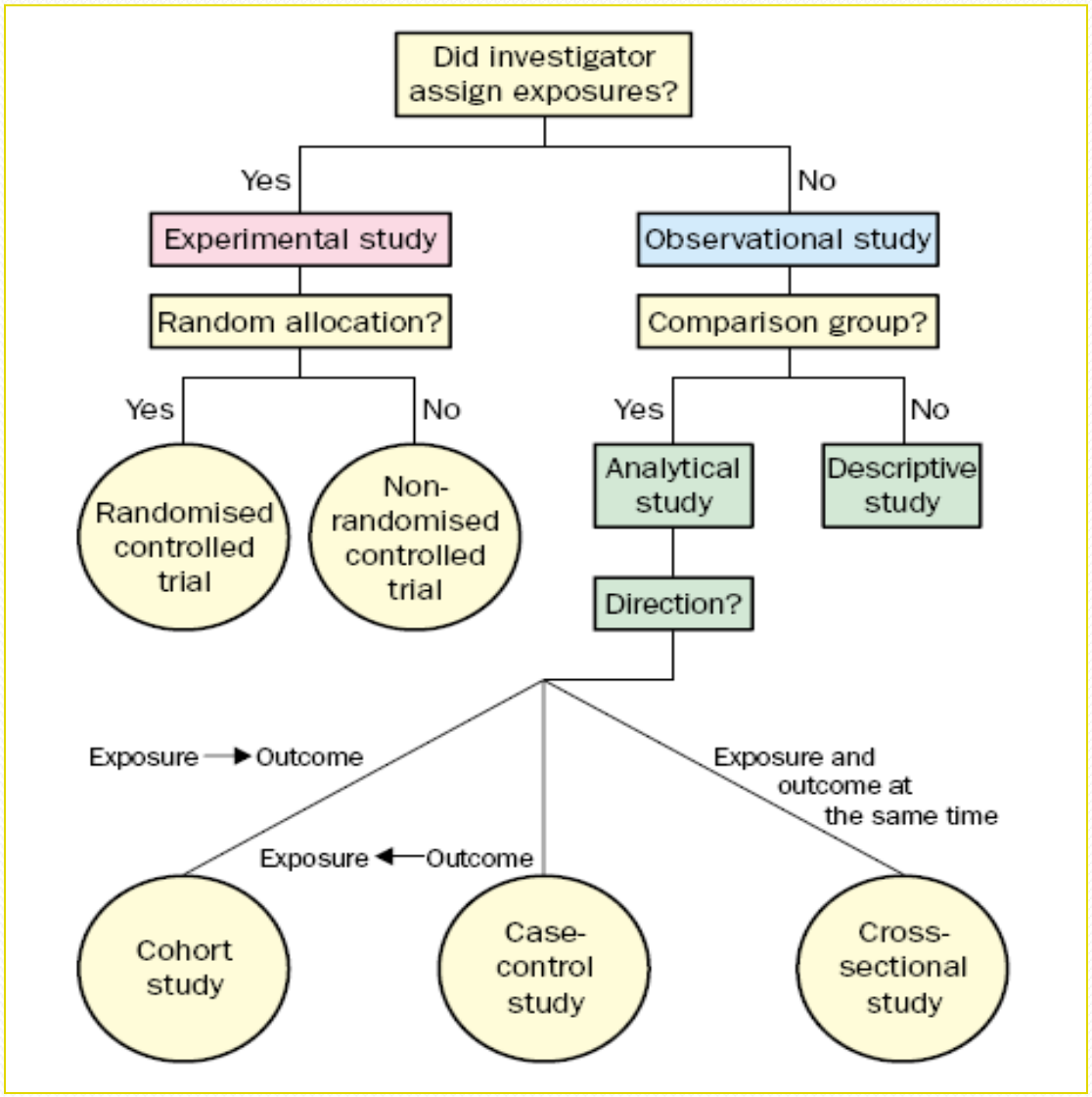
Analytical studies

Studies of suspected causes of diseases

Experimental studies

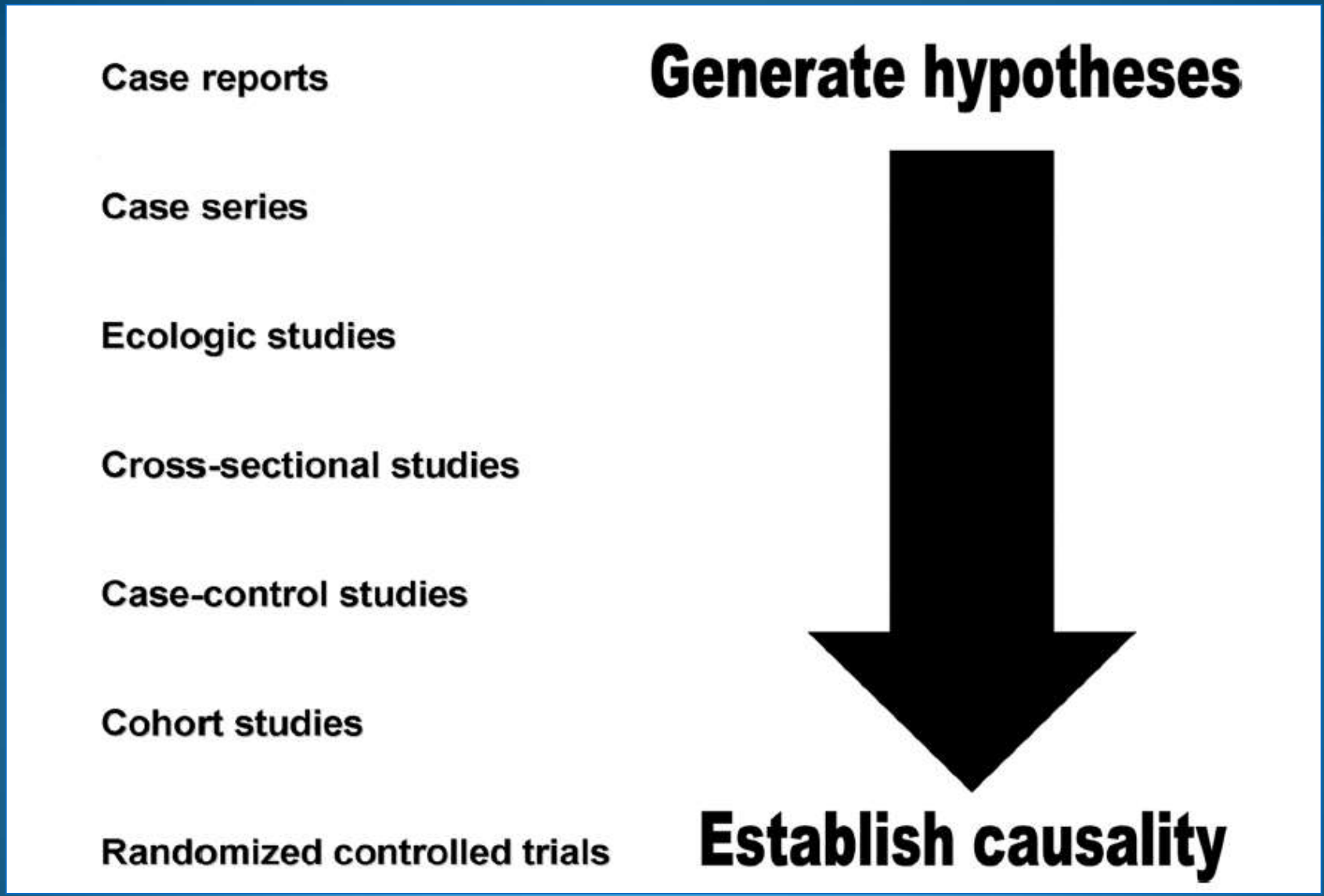
Compare treatment modalities

Epidemiologic Study Designs



Grimes & Schulz, 2002 (www)

Hierarchy of Epidemiologic Study Design



Tower & Spector, 2007 (www)

Observational Studies

(no control over the circumstances)

- **Descriptive: Most basic demographic studies**
- **Analytical: Comparative studies testing an hypothesis**
  - *** cross-sectional**
    (a snapshot; no idea on cause-and-effect relationship)
  - *** cohort**
    (prospective; cause-and-effect relationship can be inferred)
  - *** case-control**
    (retrospective; cause-and-effect relationship can be inferred)

Epidemiologic Study Designs

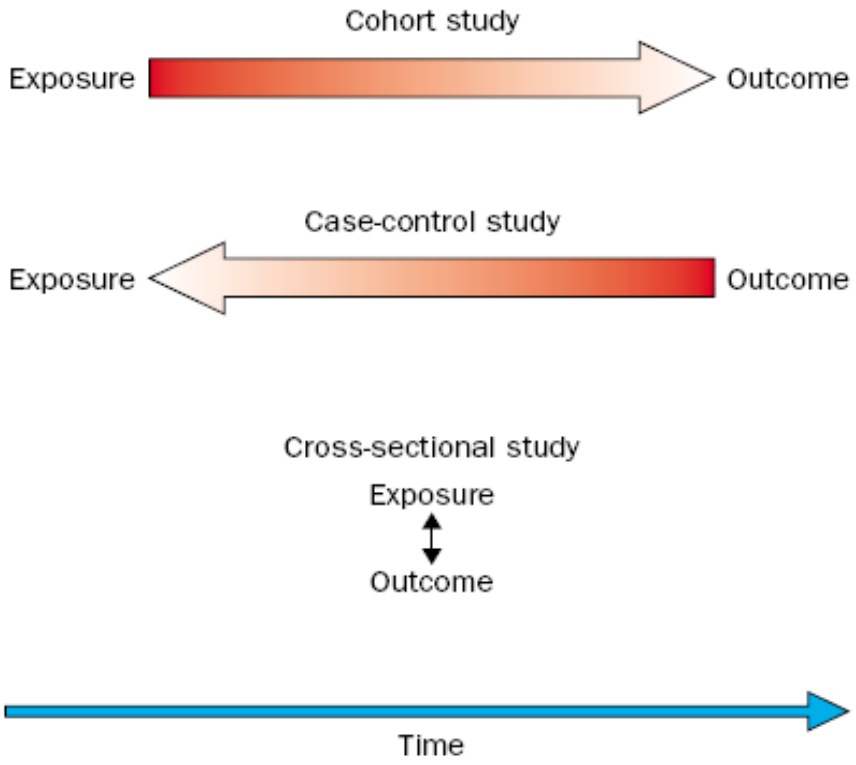


Figure 2: **Schematic diagram showing temporal direction of three study designs**

Grimes & Schulz, 2002 (www)

Analytical Studies

(comparative studies testing an hypothesis)

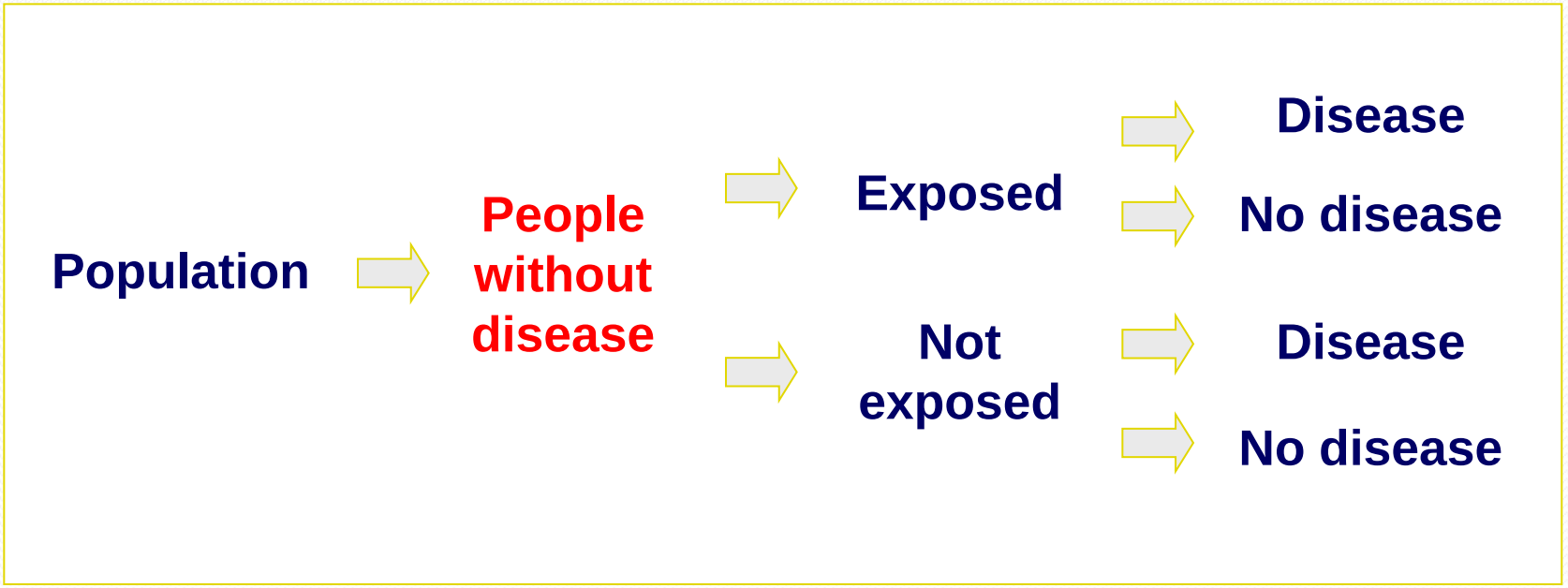
*** cohort (prospective)**

Begins with an exposure (smokers and non-smokers)

*** case-control (retrospective - trohoc)**

Begins with outcome (cancer cases and healthy controls)

Cohort Studies



Examples of Cohort Studies

* ***Framingham Heart Study*** www

* ***NHANES Studies*** www

* ***MACS*** www

* ***Physicians' Health Study*** www

* ***Nurses' Health Study*** www

* ***ALSPAC*** www

Advantages of Cohort Studies

- Can establish population-based incidence
- Accurate relative risk (risk ratio) estimation
- Can examine rare exposures (asbestos > lung cancer)
- Temporal relationship can be inferred (prospective design)
- Time-to-event analysis is possible
- Can be used where randomization is not possible
- Magnitude of a risk factor's effect can be quantified
- Selection and information biases are decreased
- Multiple outcomes can be studied
  (smoking > lung cancer, COPD, larynx cancer)

Disadvantages of Cohort Studies

- Lengthy and expensive
- May require very large samples
- Not suitable for rare diseases
- Not suitable for diseases with long-latency
- Unexpected environmental changes may influence the association
- Nonresponse, migration and loss-to-follow-up biases
- Sampling, ascertainment and observer biases are still possible

Presentation of cohort data: Population at risk

Does HIV infection increase risk of developing TB among a population of drug users?

	Population (follow up 2 years)	Cases
HIV +	215	8
HIV -	289	1

Source: Selwyn et al., New York, 1989

Does HIV infection increase risk of developing TB among drug users?

Exposure	Population (f/u 2 years)	Cases	Incidence (%)	Relative Risk
HIV +	215	8	3.7	11
HIV -	298	1	0.3	

Presentation of cohort data: Person-years at risk

Tobacco smoking and lung cancer, England & Wales, 1951

	Person-years	Cases
Smoke	102,600	133
Do not smoke	42,800	3

Source: Doll & Hill

Presentation of data: Various exposure levels

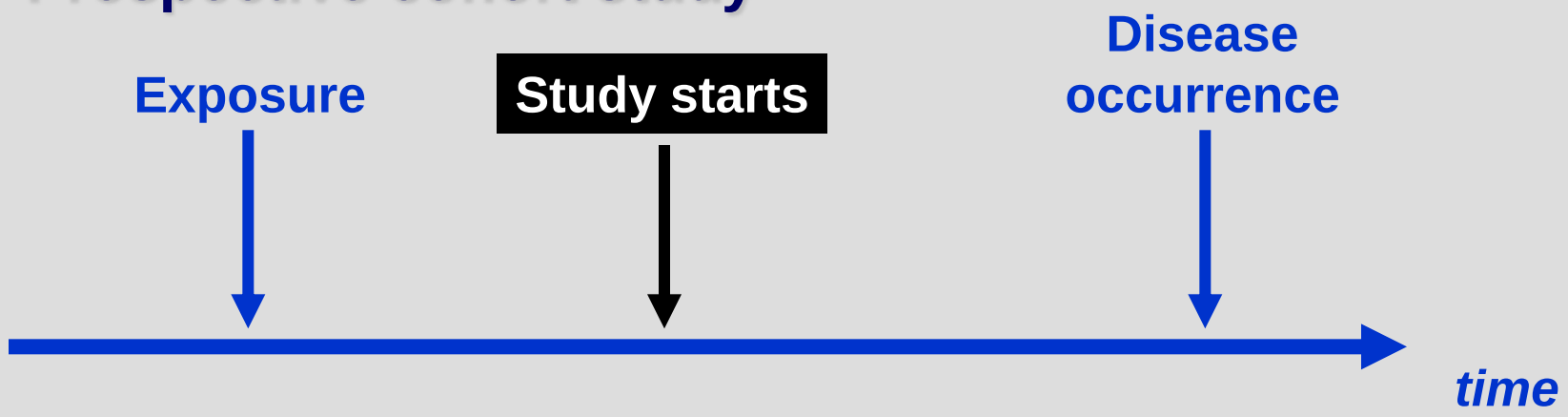
Daily number of cigarettes smoked	Person-years at risk	Lung cancer cases
> 25	25,100	57
15 - 24	38,900	54
1 - 14	38,600	22
none	42,800	3

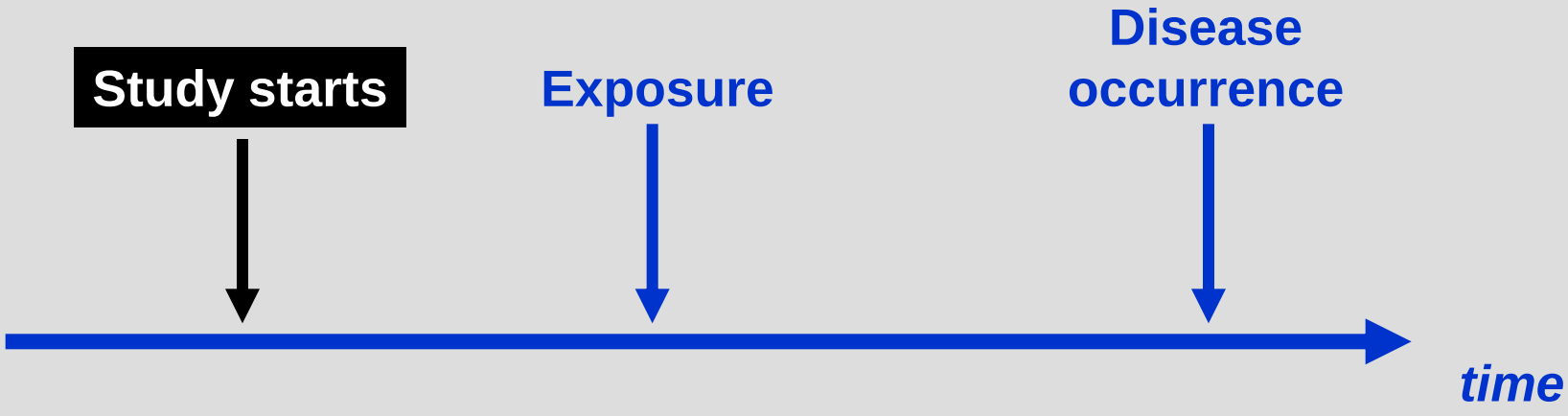
Cohort study: Tobacco smoking and lung cancer, England & Wales, 1951

Cigarettes smoked/d	Person-years at risk	Cases	Rate per 1000 p-y	Rate ratio
> 25	25,100	57	2.27	32.4
15 - 24	38,900	54	1.39	19.8
1 - 14	38,600	22	0.57	8.1
none	42,800	3	0.07	Ref.

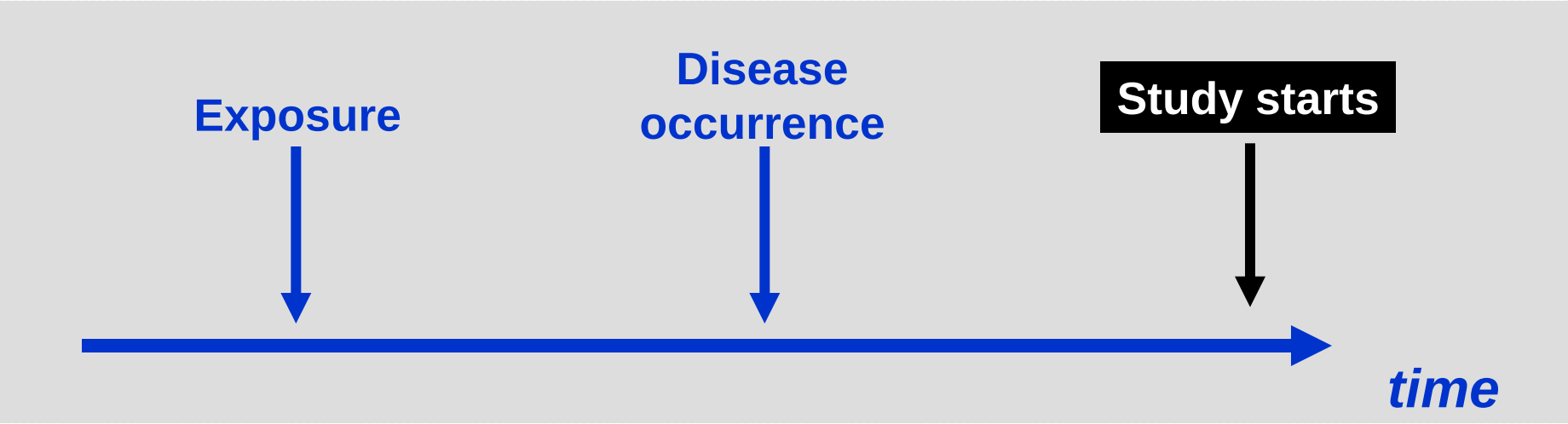
Source: Doll & Hill

Prospective cohort study





Retrospective cohort studies



Cohort Studies

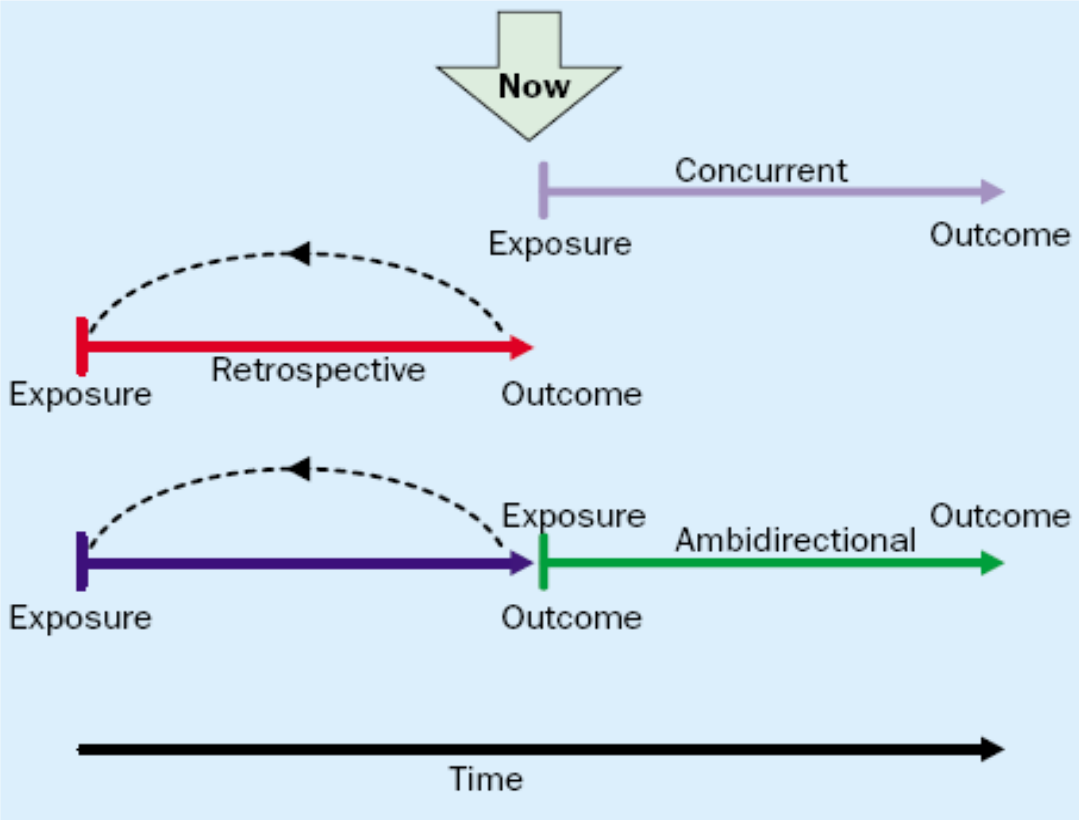
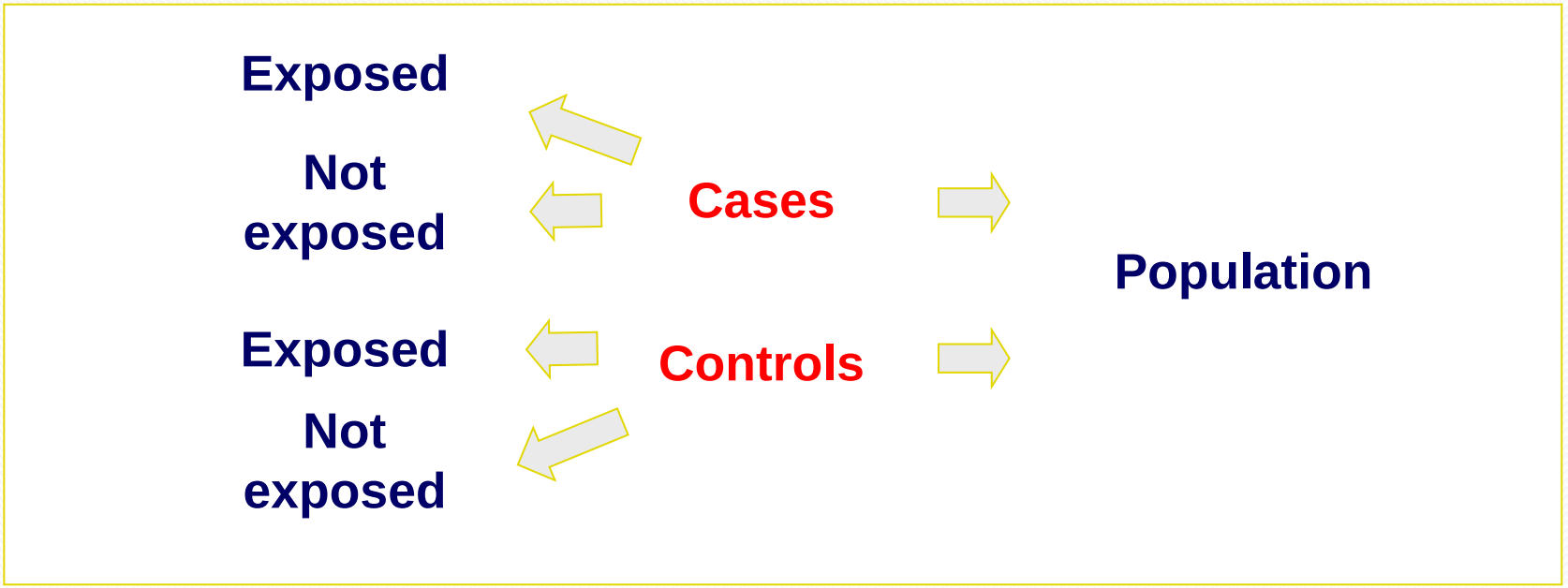


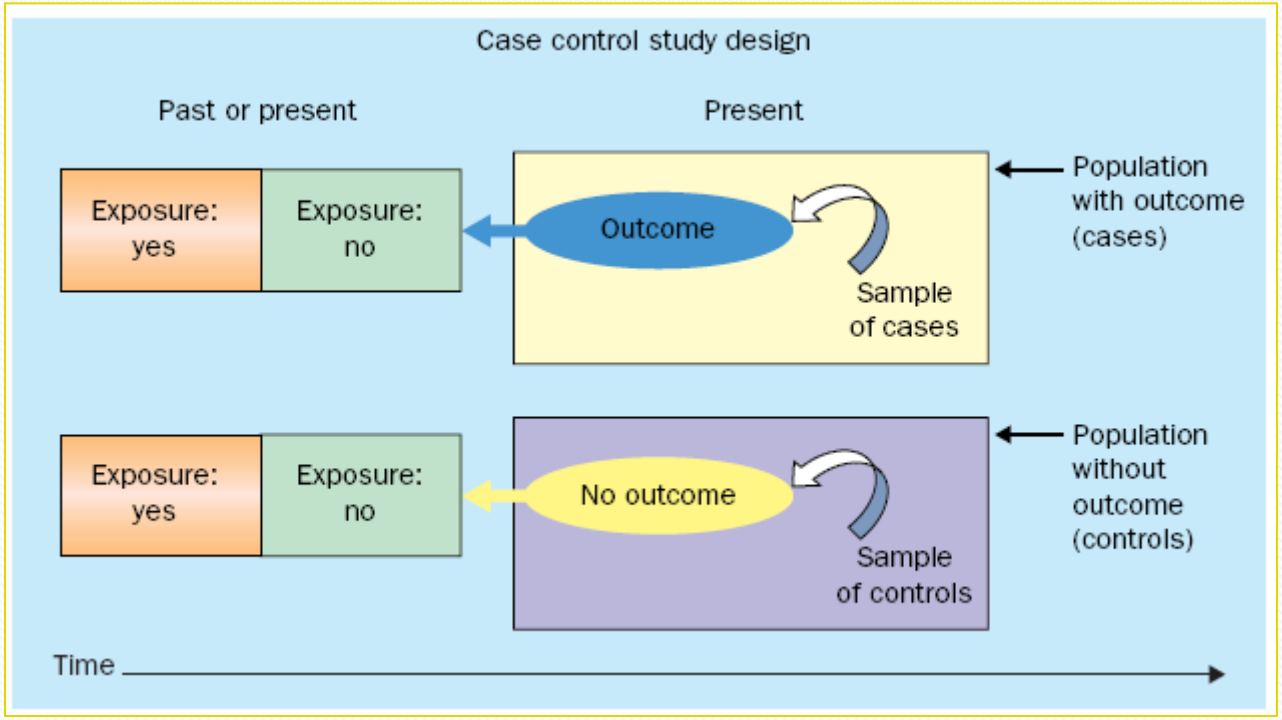
Figure 2: **Schematic diagram of concurrent, retrospective, and ambidirectional cohort studies**

Grimes & Schulz, 2002 (www) (PDF)

Case-Control Studies



Case-Control Studies



Schulz & Grimes, 2002 (www) (PDF)

Advantages of Case-Control Studies

- Cheap, easy and quick studies
- Multiple exposures can be examined
- Rare diseases and diseases with long latency can be studied
- Suitable when randomization is unethical (alcohol and pregnancy outcome)

Disadvantages of Case-Control Studies

- Case and control selection troublesome
- Subject to bias (selection, recall, misclassification)
- Direct incidence estimation is not possible
- Temporal relationship is not clear
- Multiple outcomes cannot be studied
- If the incidence of exposure is high, it is difficult to show the difference between cases and controls
- Not easy to estimate attributable fraction
- Reverse causation is a problem in interpretation - especially in molecular epidemiology studies

Case-Control Studies: Potential Bias

Panel 2: **Introduction of bias through poor choice of controls**

Cases	Control selection	Non-representativeness	Selection bias
Colorectal cancer patients admitted to hospital	Patients admitted to hospital with arthritis	Controls probably have high degrees of exposure to NSAIDs	Would spuriously **reduce** the estimate of effect (odds ratio)
Colorectal cancer patients admitted to hospital	Patients admitted to hospital with peptic ulcers	Controls probably have low degrees of exposure to NSAIDs	Would spuriously **increase** the estimate of effect (odds ratio)

NSAIDs=non-steroidal anti-inflammatory drugs.

Schulz & Grimes, 2002 (www) (PDF)

Epidemiologic Association / Impact Measures

(Absolute Risk) (AR)

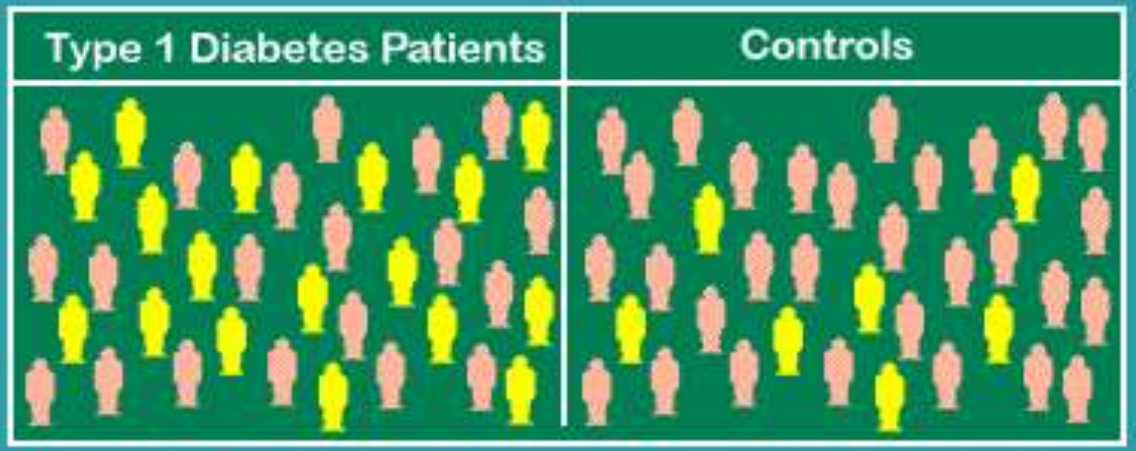
Relative Risk (Risk Ratio) (RR)

Odds Ratio (OR)

Measures of test accuracy:

Sensitivity, specificity, positive and negative predictive value (PPV, NPV)

Association Studies



Genotype	Type 1	Controls	Total
HLA DR4	17	7	24
NON-HLA DR4	20	30	50
	37	37	

$X^2_{.05} = 5.377$

$p < 0.025$

= HLA DR4

= non-HLA DR4

Odds Ratio: 3.6
95% CI = 1.3 to 10.4

ROCHE Genetic Education (www)

Genotype	Type 1	Controls	Total
HLA DR4	17	7	24
NON-HLA DR4	20	30	50
	37	37	

a = 17
b = 20
c = 7
d = 30

OR = ad / bc = 17*30 / 20*7 = 3.6
RR = (a/(a+c)) / (b/(b+d)) = (17/24)/(20/50) = 1.8

EBM toolbox (www)
EpiMax Table Calculator (www)

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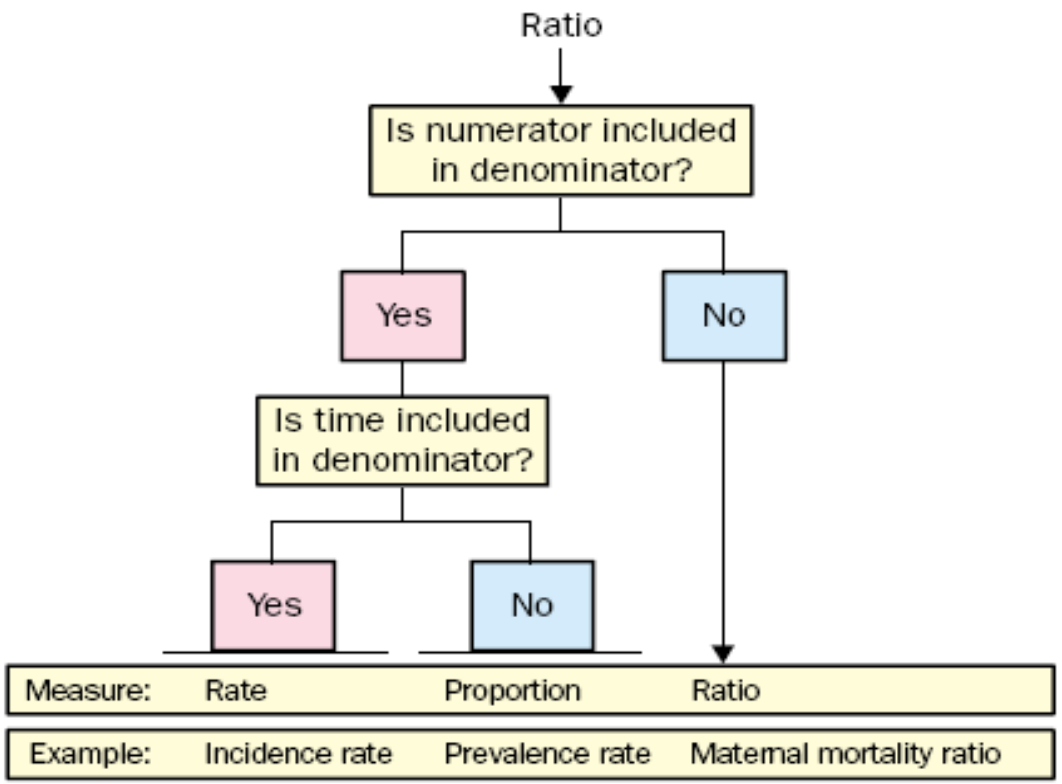

Figure 3: **Algorithm for distinguishing rates, proportions, and ratios**

Grimes & Schulz, 2002 (www)

Sources of Error in Epidemiologic Studies

Random error

Bias

Confounding

Effect Modification

Reverse Causation

Sources of Error in Epidemiologic Studies

Random error

Large* sample *size, replication

Bias

Be careful

Confounding

Effect Modification

Reverse Causation

Confounding can be controlled by:

- **Randomization**: assures equal distribution of confounders between study and control groups

- **Restriction**: subjects are restricted by the levels of a known confounder

- **Matching**: potential confounding factors are kept equal between the study groups

- **Stratification** for various levels of potential confounders

- **Multivariable analysis** (does not control for *effect modification*)

Effect modification can be assessed by:

- **Stratification** for various levels of potential confounders
- **Multivariable analysis** (by assessing interaction)

Reverse causation can be assessed by:

- **Mendelian Randomization**

Thank you