



Observational Studies



PhUSE US Connect 2018

June 2018 / Anupama Sheoran / Lead Stat
Analyst / Bayer



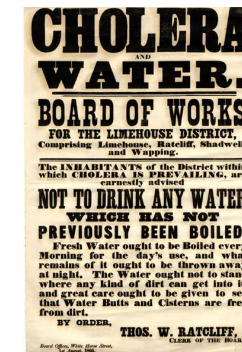
Agenda

- **Study designs for
Observational studies and data
sources**
- **Study types – overview &
explanation**
- **Data sources & databases**
- **Key steps in designing
Observational studies**

Background

Epidemiology is defined as the study & analysis of the distribution (frequency, pattern) and determinants (causes, risk factors) of health & disease frequency in defined human populations.

(Hennekens C. Epidemiology in Medicine, 1987)



Pharmacoepidemiology is defined as the study of the use and effects of drugs in large numbers of people (Strom B.L. 1989)

Pharmacoepidemiology applies epidemiological methods to studies of the clinical use of drugs in populations





A Rapidly Changing Environment

2000

- Increasing interest in real world data also by **payers and patients** (e.g. NICE 2004)

2005

- Expanded use of healthcare databases with development of **distributed data networks** and increasing use of **novel analytical tools** (e.g. Sentinel FDA)

2008

- Increasing importance of public private consortiums and partnerships (e.g. Innovative Medicine's Initiative)

2012

- **Regulators and payers** defining ways to jointly assess the safety and effectiveness of drugs (e.g. EunetHTA)

2015

- Increasing interest in use of **observational data for key decision-making by regulators and payers**. Use of **novel, hybrid designs, data sources**

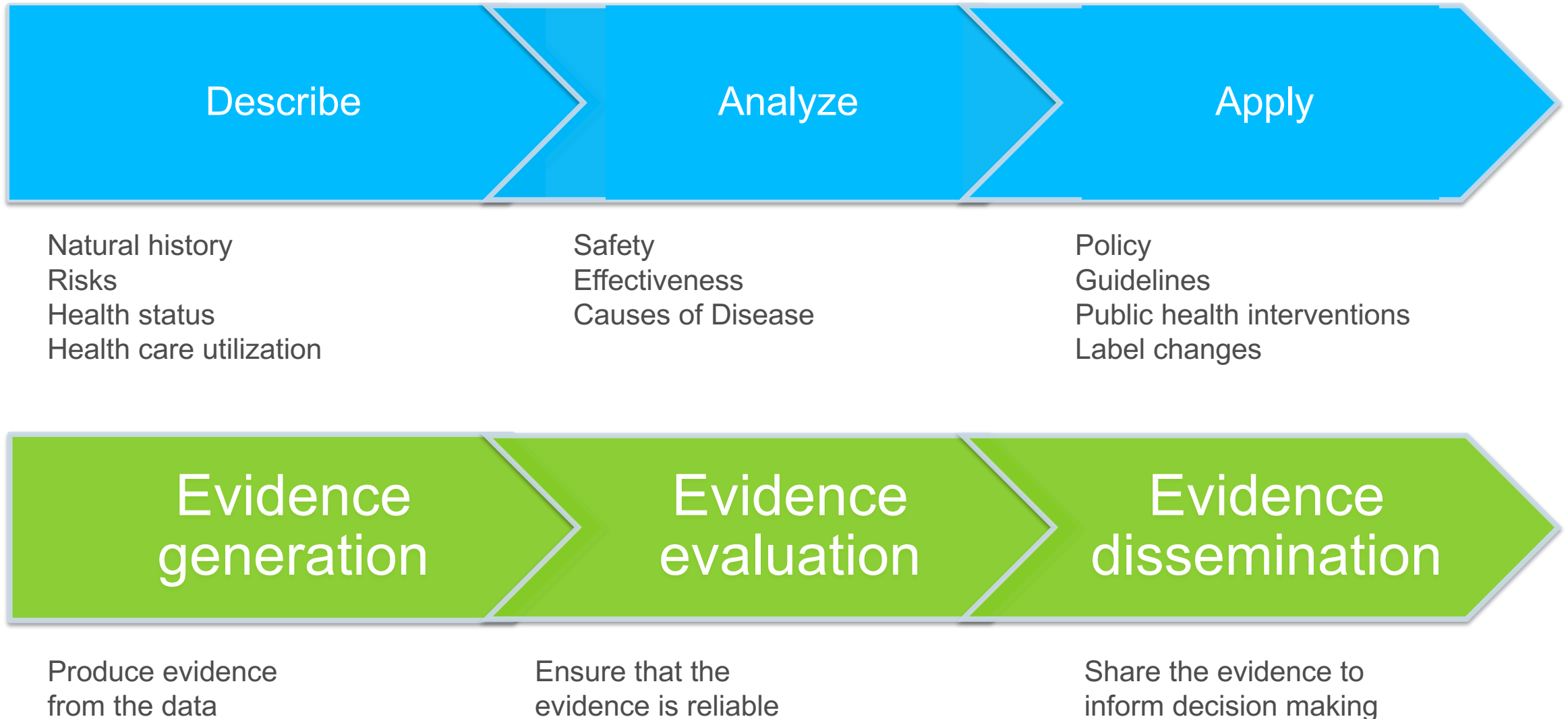
2016

- Interest in applying real-world data to drug development got a major boost with the passage of the **21st Century Cures Act in 2016**

Objectives of Observational Studies

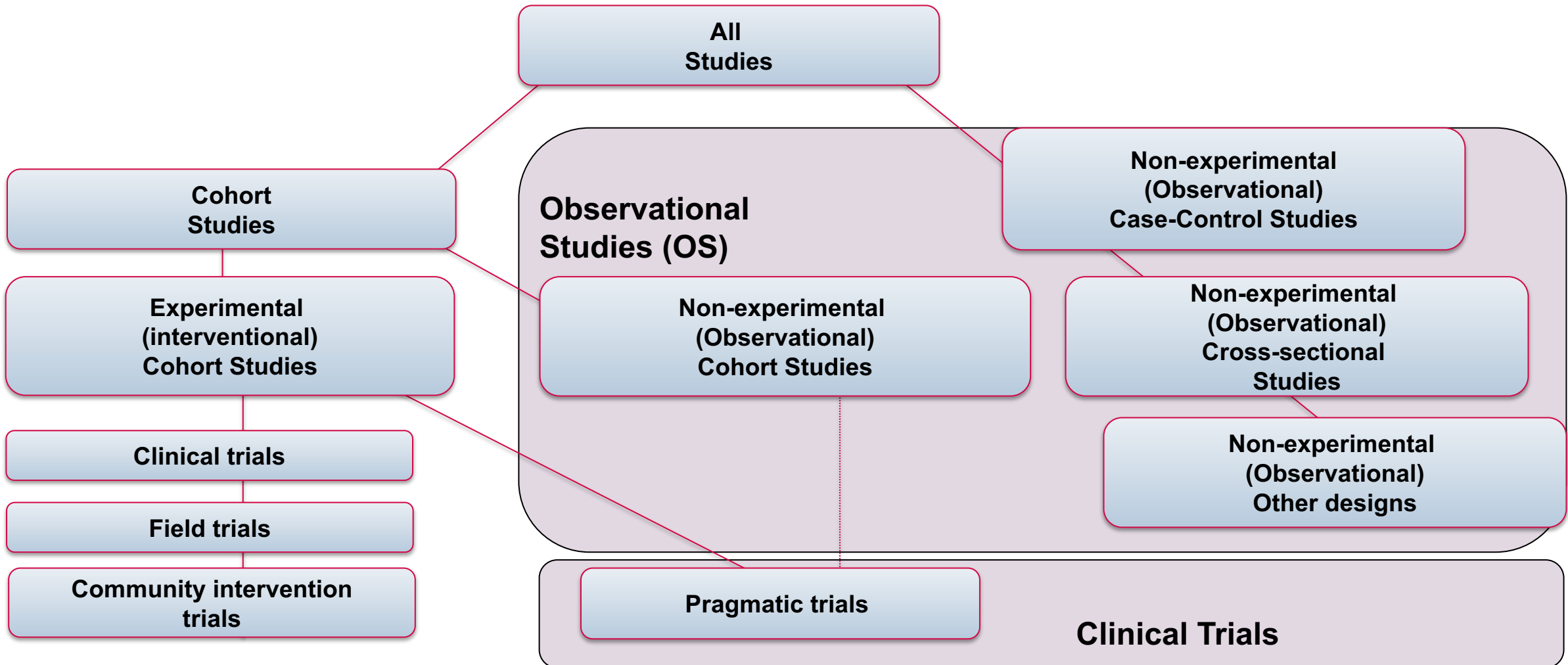


Objectives of Observational Studies

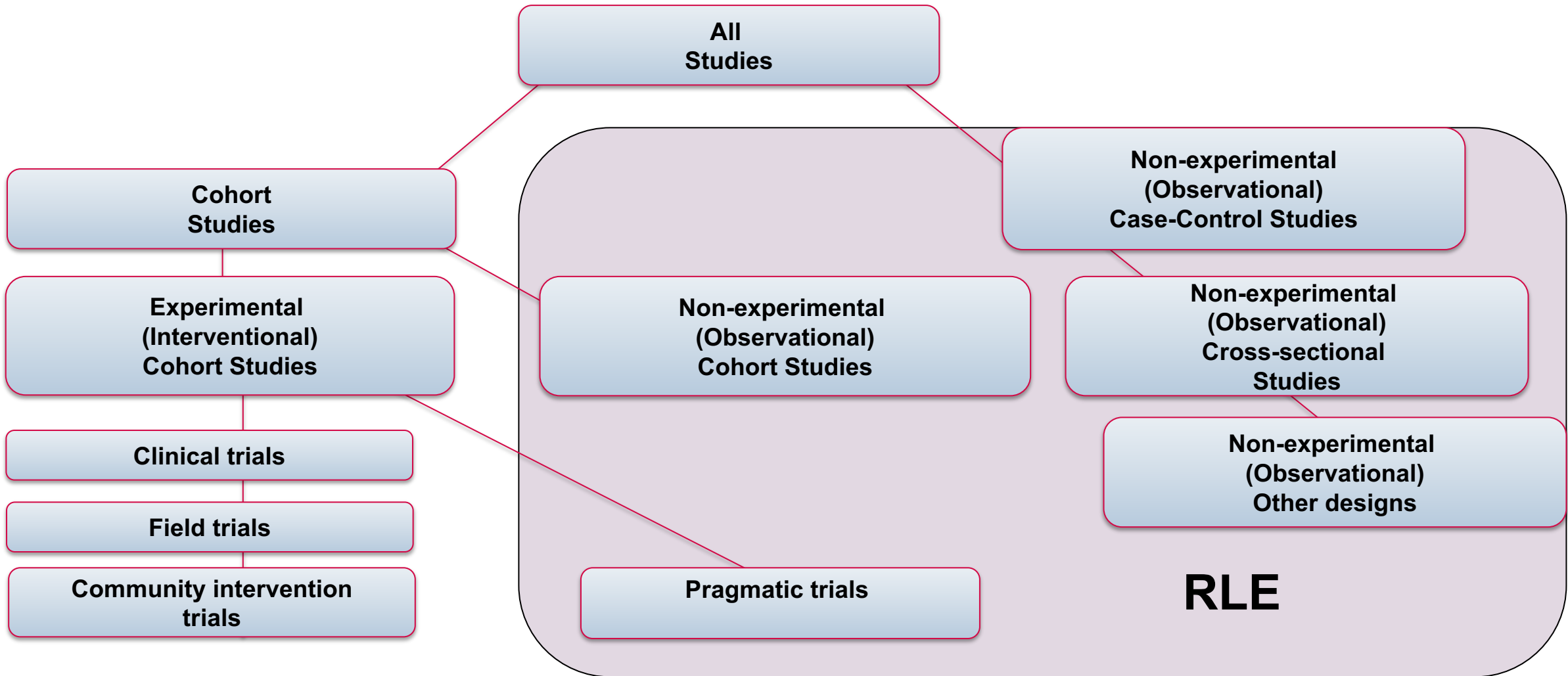


What are the study designs/types and data sources used in Observational Studies?

Study Designs

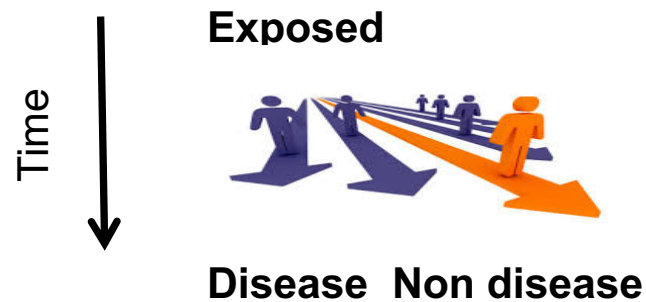


Study Designs



Cohort Study

- Any designated group of individuals who are followed or traced over a period of time
- Comprises persons with a common baseline characteristic
- Cohorts are often defined according to their level of exposure to a drug or intervention
- Measures the occurrence of disease within one or more cohorts



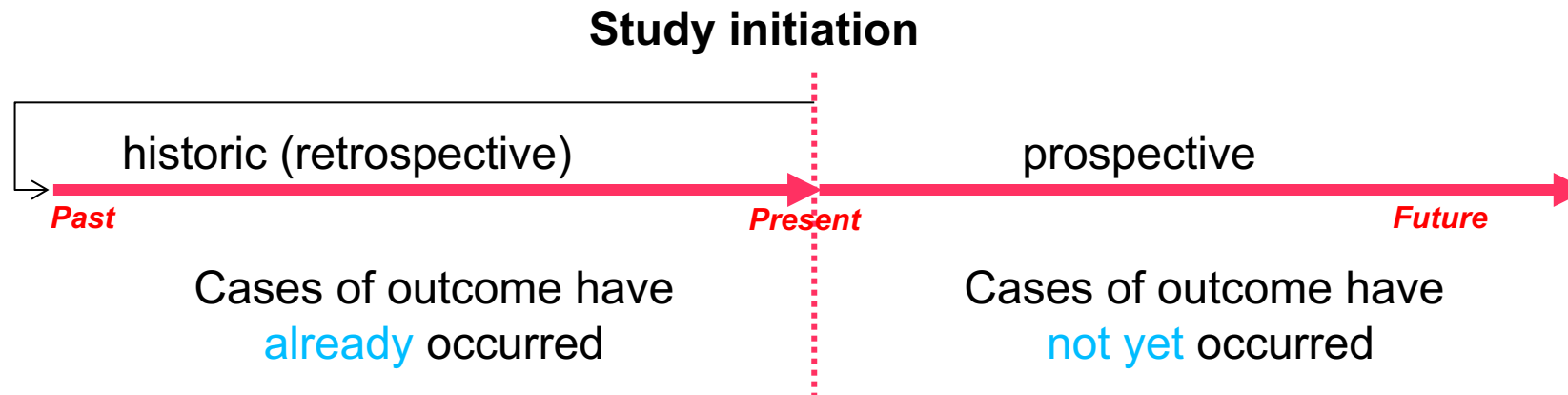
Choice of comparison group in a cohort study

The ideal comparison group (unexposed) in a cohort study consists of individuals who are identical to those exposed in all aspects except the exposure of interest



Cohort Study Types

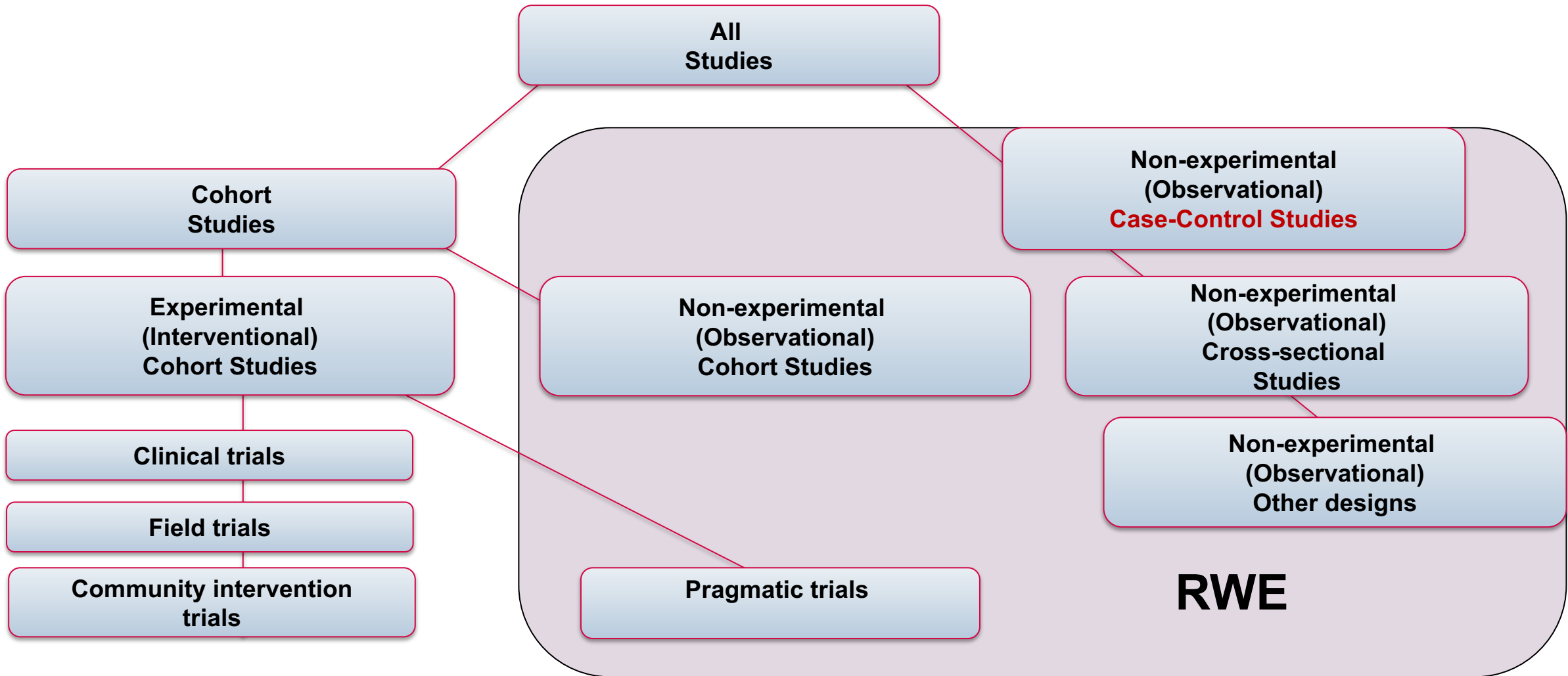
1. Prospective vs. retrospective cohort study



2. Closed vs. dynamic (open) cohort study

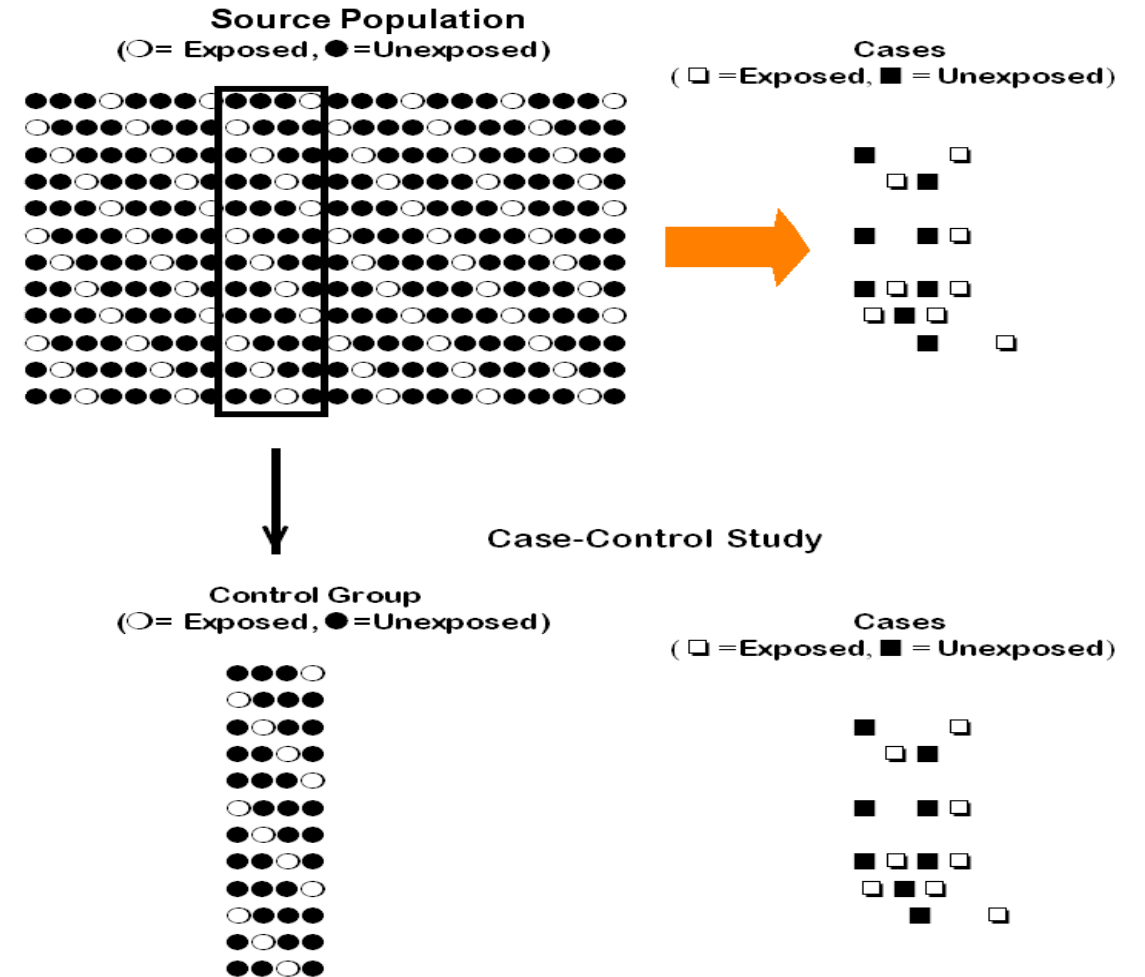
- Closed cohort:
 - No members added during the period of follow-up
 - No losses other than due to the outcome event
- Dynamic (open) cohort:
 - New members can enter and move out during follow-up
 - Loss of follow-up may occur

Epidemiological Study Designs



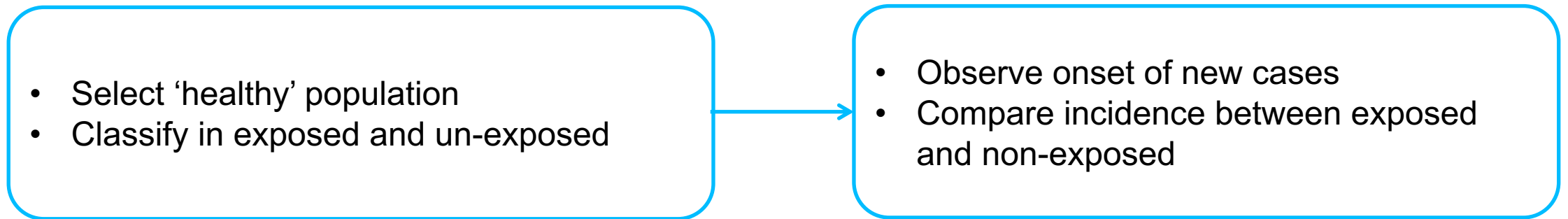
Case-Control Study

- Compare cases with the disease with controls without the disease
- Looking for differences in antecedent exposures
- The control group is chosen from the same population that gave rise to the cases
- Controls are sampled independently of their status regarding the exposure of interest

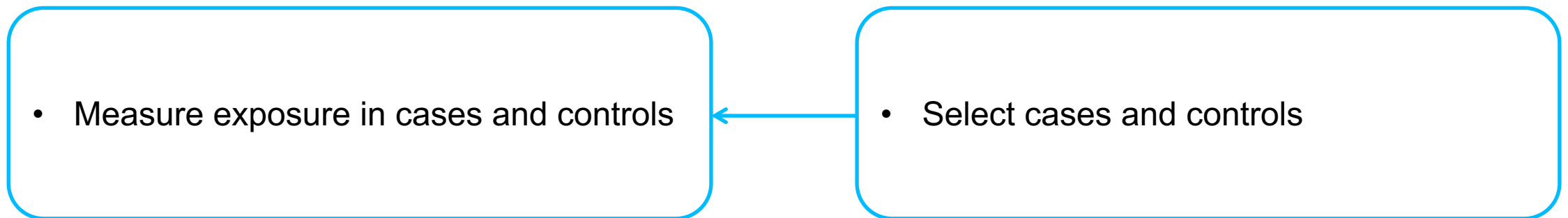


Cohort Study vs. Case-Control Study

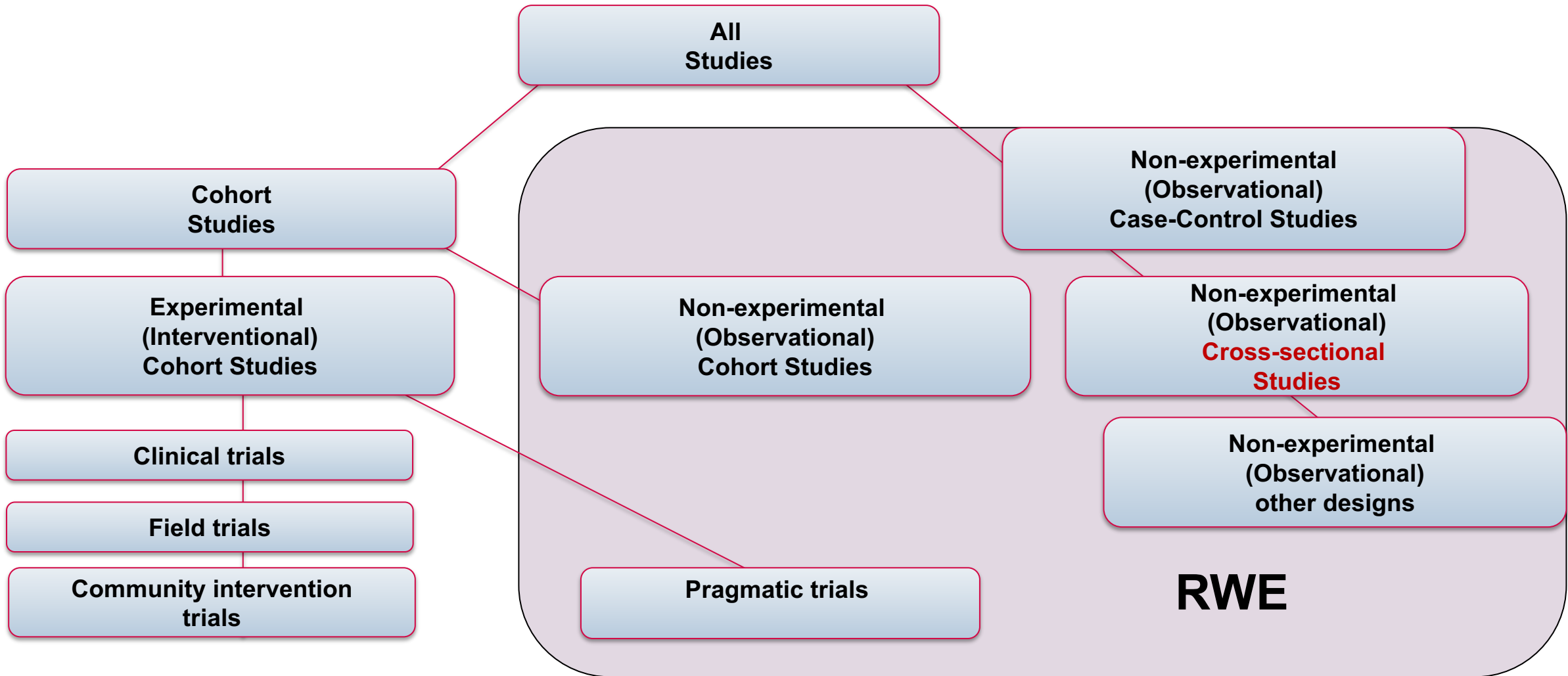
Cohort Study



Case-control Study



Study Designs



Cross-Sectional Studies (Surveys)

A cross-sectional study includes as subjects

- all persons in a population
- or a representative sample of the population at the time of ascertainment, without regard to exposure or disease status

The cross-sectional design provides a 'snapshot' of the population status at a specific point in time

- with respect of disease
- or exposure variables
- or both



What are the Main data sources used in Observational Studies?

Potential Data Sources for Observational studies

Primary data :

Primary data are collected by the investigator directly from study participants to address a specific question or hypothesis. Data can be collected by in-person or telephone interviews, mail surveys, or computerized questionnaires

- **Longitudinal field studies**
- **De novo registries**
- **Surveys**
- **Patient reported outcomes**



Potential Data Sources for Observational studies

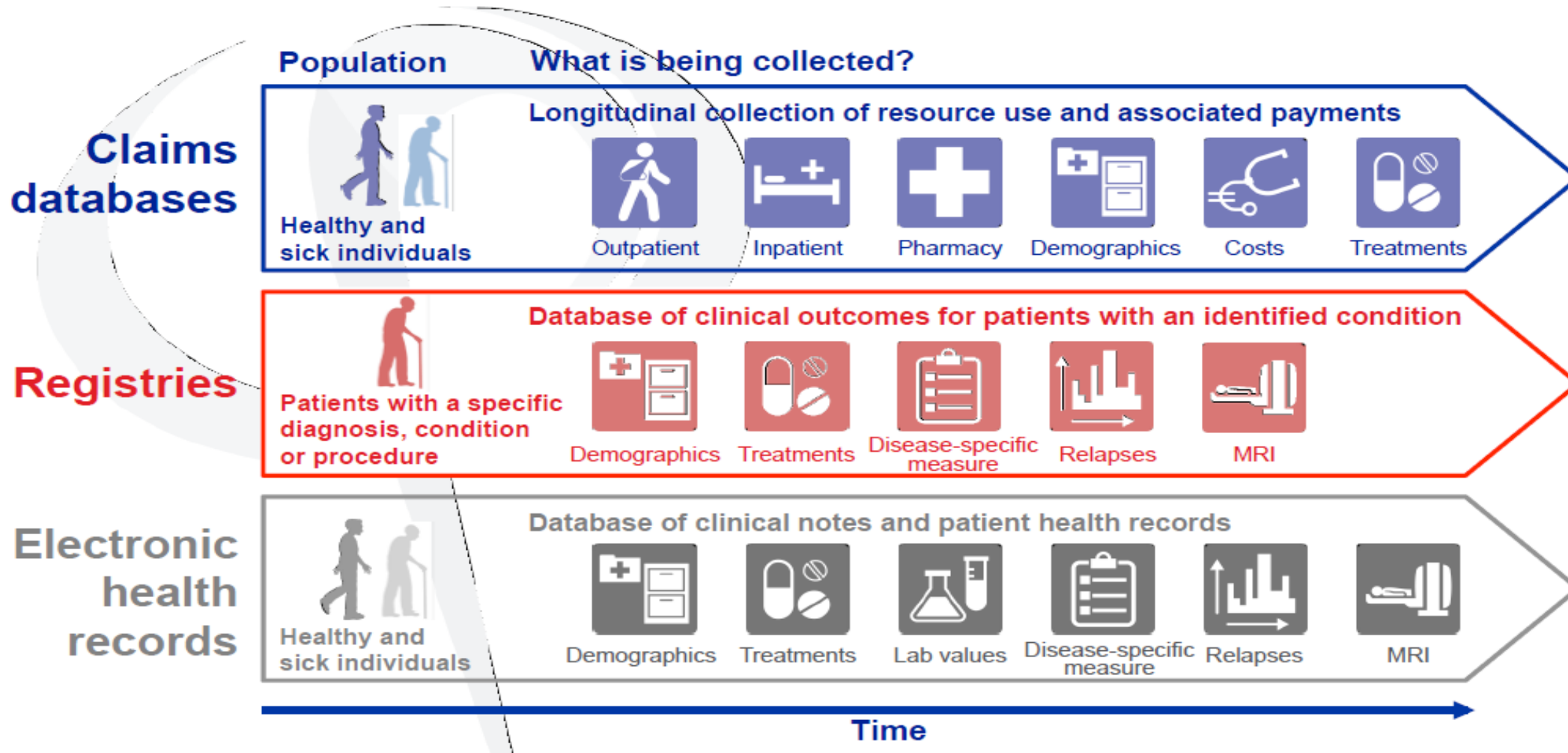
Secondary data :

Data are gathered during patient care, which is the primary purpose of the data being generated. Depending on their primary purpose, secondary data have various formats.

- Data are obtained from the review of paper-based or electronic medical records (EMRs), from health insurance claims for services provided, laboratory results and pharmacy dispensings databases, disease and drug registries



Potential Data Sources for Observational studies



Potential Data Sources for Observational studies

Secondary data :

Electronic healthcare databases

- Primary care records
- Hospital records

Administrative databases

- Insurance claims records

Pharmacy record databases

Paper-based records

Existing registries

- Cancer registries
- Rare disease registries

Death registries

Census data



Data linkage

Examples of Secondary data sources

Administrative databases (claims databases), e.g.:

- Saskatchewan database (Canada)
- MarketScan and Optum (USA)
- GePaRD (Germany)
- SNIIRAM (France)

Physician-based databases (medical records databases), e.g.:

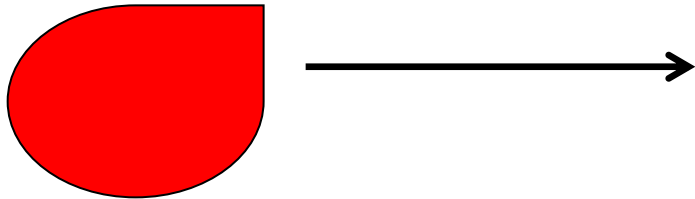
- CPRD (former GPRD, UK)
- THIN database (UK)
- Kaiser Permanente (USA)

What are the key steps in designing Observational Studies?

Key Steps to Follow when Designing an Observational Study (Real Life Evidence Generation)



Question development:



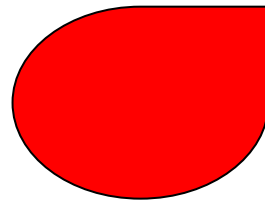
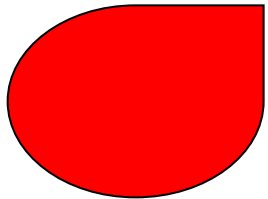
Carefully define the scientific question

Consider up-front potential challenges including sources of bias and ways to prevent/control them

Key Steps to Follow when Designing an Observational Study (Real Life Evidence Generation)



Question development



Data sources evaluation



Explore data options and availability of information (exposure, outcomes, covariates etc.)

- Existing data sources (secondary data source)
- New data sources (primary data source)

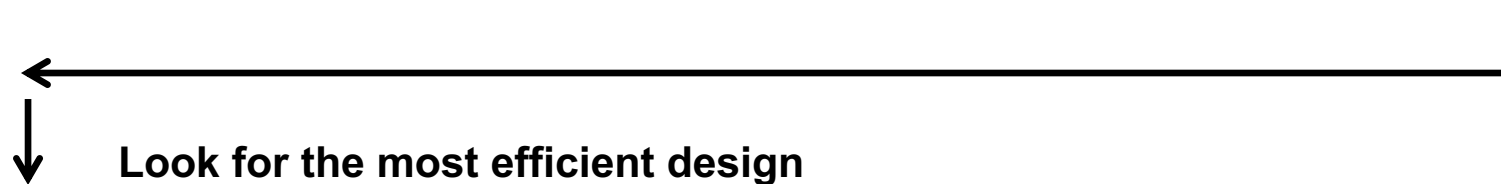
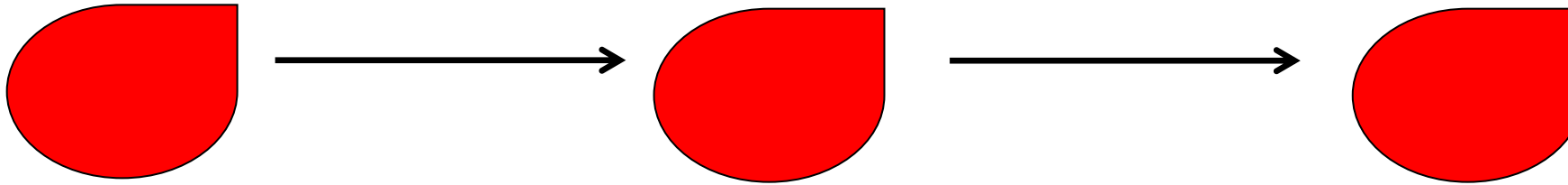
Key Steps to Follow when Designing an Observational Study (Real Life Evidence Generation)



Question development

Data sources evaluation

**Research approach
definition**



Look for the most efficient design

Consider all options

Ideally include a comparison group

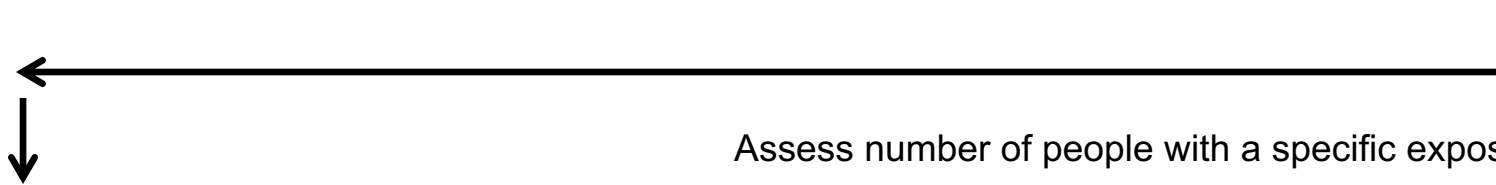
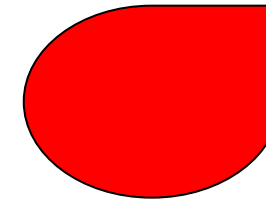
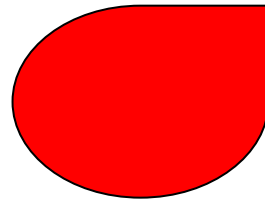
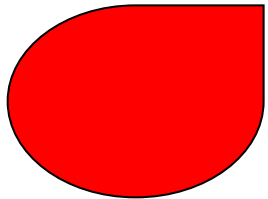
Key Steps to Follow when Designing an Observational Study (Real Life Evidence Generation)



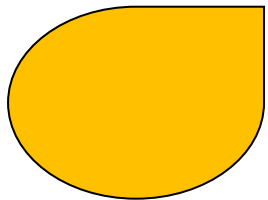
Question development

Data sources evaluation

Research approach definition



Feasibility assessment

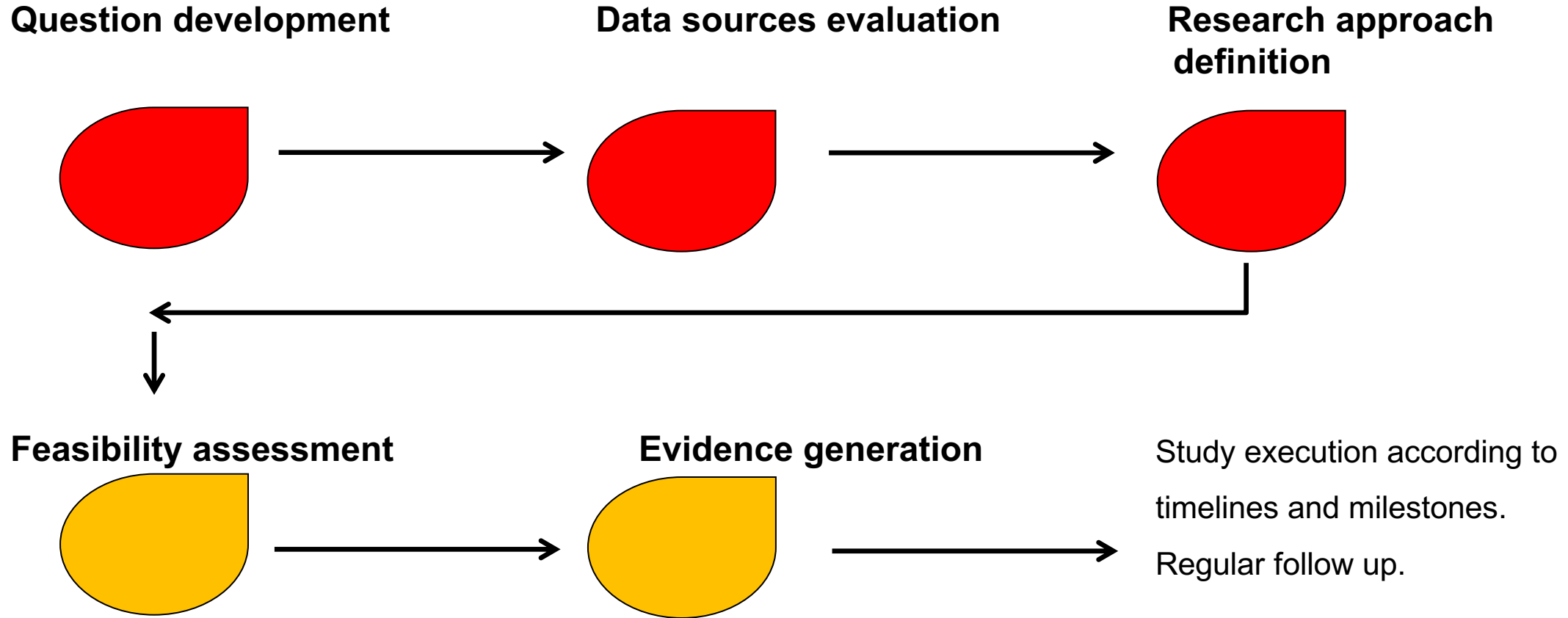


Assess number of people with a specific exposure or outcome, the availability of covariates and follow up period. Validate diagnosis, procedures, outcomes.

Conduct operational feasibility.

Determine whether the data source could answer the research questions within the expected timelines and with the required statistical power for the proposed study design.

Key Steps to Follow when Designing an Observational Study (Real Life Evidence Generation)



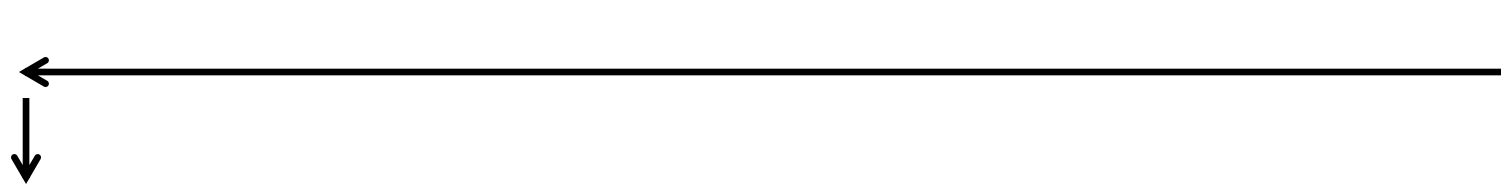
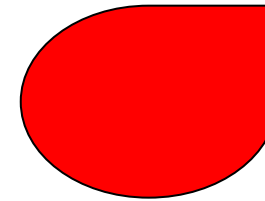
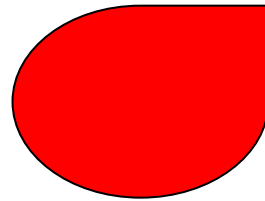
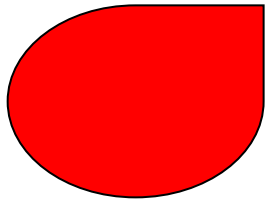
Key Steps to Follow when Designing an Observational Study (Real Life Evidence Generation)



Question development

Data sources evaluation

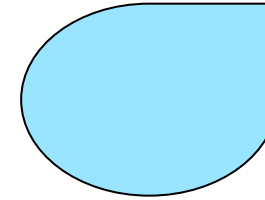
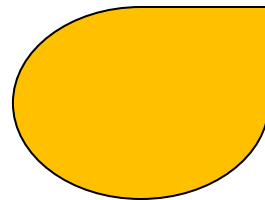
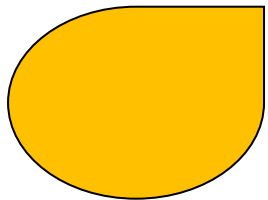
**Research approach
definition**



Feasibility assessment

Evidence generation

Evidence dissemination



Use of evidence for
decision-making. Study
report, scientific
publications



Q & A Session



Thank you!

