Overview of study designs I
Observational descriptive studies

Part 1:

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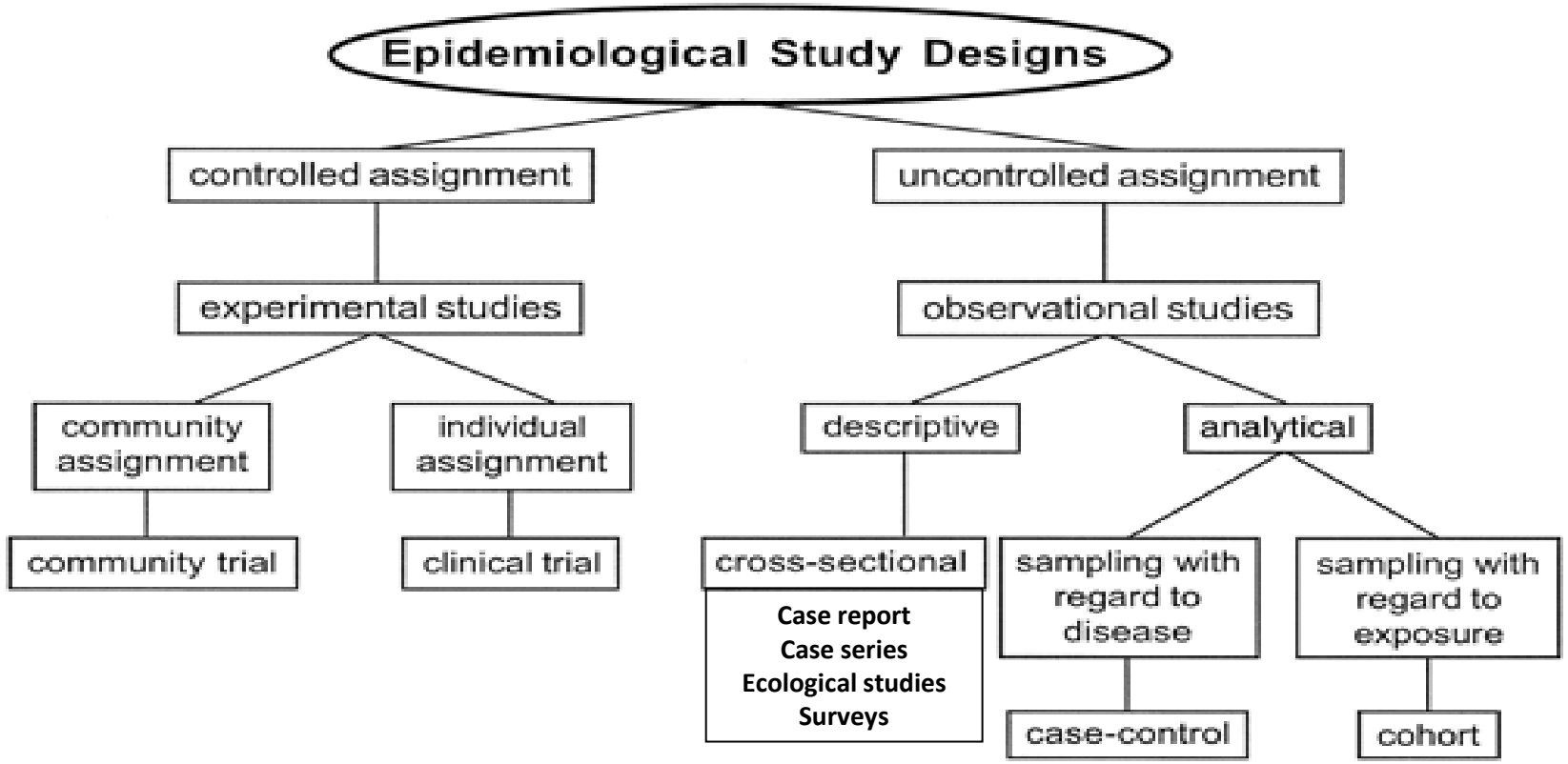
Part 1

Descriptive studies

Study design: Definition

A study design is a specific plan or protocol for conducting the study, which allows the investigator to translate the conceptual hypothesis into an operational one.



Source: Waning B, Montagne M: *Pharmacoepidemiology: Principles and Practice*: http://www.accesspharmacy.com

Observational epidemiology

- Provides information about disease patterns or drug use problems by various characteristics of person, place, and time.

- It also is used by epidemiologists to generate hypotheses regarding the causes of disease or drug use problems.

Controlled versus uncontrolled assignment

- Aspirin for prevention of colorectal cancer
- It can be a cohort study: Uncontrolled assignment for patients who are taking Aspirin for different indications
- It can be a randomized controlled clinical trial where we allocated patients to take Aspirin or Placebo

Observational epidemiology

a. Descriptive

Case reports and case series

Descriptive analysis (Person place time)

Ecological (correlational)

Cross-sectional

b. Analytical

Case Control

Cohort

Epidemiological studies

- Observational studies are descriptive or analytical in nature.

- Descriptive studies attempt to uncover and portray the occurrence of the condition or problem, whereas analytical studies determine the causes of the condition or problem.
- Investigators in observational studies may plan and identify variables to be measured, but human intervention is not a part of the process.
- Experimental studies, in contrast, involve intervention in ongoing processes to study any resulting change or difference.

Observational epidemiology

- Descriptive studies: provide insight, data, and information about the course or patterns of disease or drug use problems in a population or group.

- Analytical studies are used to test cause–effect relationships, and they usually rely on the generation of new data.

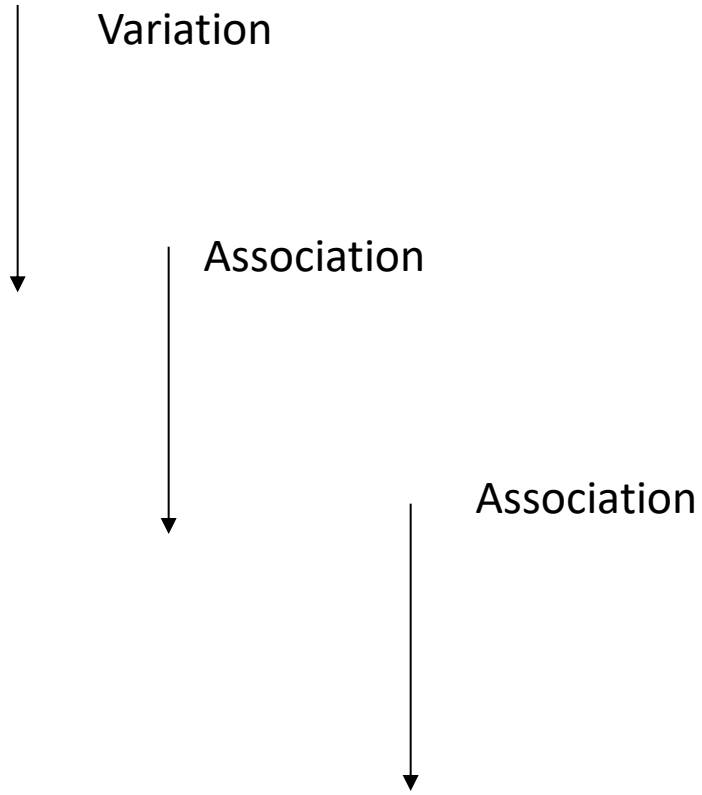
Epidemiological studies

Clinical observation

Descriptive studies

Analytical studies

Experimental studies



Does coffee causes pancreatic cancer

I am beginning to suspect that there is an association between coffee drinking and pancreatic cancer ……

I have seen a good number of cervical cancer patients positive for HPV…

Case series

Descriptive analysis

Ecological study

Cross-sectional analysis

How to investigate this further?

Prospective vs. retrospective studies

Prospective studies

- Watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s).
- The outcome of interest should be common; otherwise, the number of outcomes observed will be too small to be statistically meaningful (indistinguishable from those that may have arisen by chance).

- All efforts should be made to avoid sources of bias such as the loss of individuals to follow up during the study.

- Prospective studies usually have fewer potential sources of bias and confounding than retrospective studies.

Retrospective studies

- **A looks backwards and examines exposures to suspected risk or protection factors in relation to an outcome that is established at the start of the study.**
- **Many valuable case-control studies, such as Lane and Claypon's 1926 investigation of risk factors for breast cancer, were retrospective investigations.**
- **Confounding factors and bias are more common in retrospective studies than in prospective studies.**

Comparison of Retrospective and Prospective Approaches	
Retrospective	**Prospective**
Inexpensive to conduct	Expensive to conduct
Completed in a shorter time period	Completed over a longer time period
Easier to access a larger number of subjects	More difficult to access subjects and usually requires a larger number of subjects
Allows results to be obtained more quickly	Exposure status and diagnostic methods for disease may change
Useful for studying exposures that no longer occur	Loss of subjects from the study over time may be substantial
Information and data may be less complete and inaccurate	Information and data may be more complete and accurate
Subjects may not remember past information	Direct access to study subjects enhances reliability of data

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Case Reports and Case Series

Case report is detailed report by one or more clinicians of the profile of a single patient.

Example: 1961; pulmonary embolism 5 weeks after use on oral contraceptive.

Question: Are women who develop pulmonary embolism more likely to have used oral contraceptives than women who did not develop the disease?

Case Series describes the characteristics of a number of patients with a given disease.

Application: Routine surveillance activities (accumulated case reports). Striking clustering of cases may suggest emergence of new diseases or epidemics

Case report and case series

- **Clinician finds unusual features of a disease or effects of a drug, or the patient's medical history, that lead to the formulation of a new research question or hypothesis**

Hammade et al.
Journal of Medical Case Reports (2022) 16:386
https://doi.org/10.1186/s13256-022-03630-1

Journal of
Medical Case Reports

CASE REPORT Open Access

Isolated giant renal hydatid cyst with a simple renal cyst appearance: a case report

Mohammed Hammade[1*], Sami Alhoulaiby[1] and Adnan Ahmed[2]

Abstract

Background: Isolated renal hydatid cysts of the kidney are a rare occurrence that account for about 2–3% of all hydatidoses. They can stay asymptomatic for years and could have a variable presentation on imaging techniques, which results in a challenging diagnostic process.

Case presentation: We report a 22-year-old Caucasian male with a large cyst on the upper pole of the left kidney that had no septations nor membrane calcifications on computed tomography, which led to mistakenly considering it a simple renal cyst. The true diagnosis was identified intraoperatively and proven postoperatively by pathology.

Conclusions: This case highlights the importance of keeping echinococcosis in mind when treating suspected renal cysts and tumors to avoid incorrect treatment and possible content spillage, anaphylaxis, and peritoneal dissemination.

Keywords: Isolated renal hydatid cyst, Renal echinococcosis

Case Reports Transpl Int
. 2002 Jul;15(7):374-6. doi: 10.1007/s00147-002-0426-9. Epub 2002 Jun 20.

Colchicine myoneuropathy in a renal transplant patient

Peter Dupont 1, Ian Hunt, Lawrence Goldberg, Anthony Warrens
Affiliations expand

PMID: 12122515 DOI: 10.1007/s00147-002-0426-9

Abstract
Colchicine is widely employed for the treatment of gout in renal transplant patients where NSAIDs are contra-indicated and allopurinol prophylaxis is often avoided due to concomitant azathioprine immunosuppression. We report here a case of colchicine-induced myoneuropathy in a renal transplant recipient. Our patient had myalgia, muscle weakness, elevated creatine kinase levels, myopathic changes on electromyography and peripheral neuropathy. Withdrawal of colchicine resulted in recovery within 4 weeks. Renal transplant recipients are likely to be at greater risk of colchicine-induced myoneuropathy due to the unique concurrence of risk factors predisposing to toxicity in such patients. These risk factors include the high incidence of gout in this population, widespread use of colchicine as first-line therapy, impaired renal function and concomitant cyclosporin treatment. The diagnosis should be considered in any renal transplant recipient receiving the drug who develops myopathy. Prompt withdrawal of colchicine therapy should result in rapid clinical and biochemical improvement.

Case reports

- The most common type of study published in the medical literature.
- They note unusual medical occurrences, identify new diseases, and describe adverse effects from drug therapies.

- Clinical investigators can use challenge–rechallenge data to help establish causality.
- In this approach, administration of a drug (the challenge) might be suspected of producing a specific symptom (side effect or adverse reaction).
- Administration of the drug can be stopped to observe whether the side effect or adverse reaction diminishes.
- If it does, then administration of the drug can be resumed (the rechallenge) to observe whether the effect returns, suggesting a possible relationship between the two events.

Case-series:
Clinical case series

- Usually a coherent and consecutive set of cases of a disease (or similar problem) which derive from either the practice of one or more health care professionals or a defined health care setting, e.g. a hospital or family practice.

Clinical Neurology and Neurosurgery
Volume 99, Issue 4, December 1997, Pages 266-270
Clinical Neurology and Neurosurgery
Case report

Acute onset of colchicine myoneuropathy in cardiac transplant recipients: case studies of three patients

Author links open overlay panel Sandeep S Rana a, Michael J Giuliani a, Chester V Oddis b, David Lacomis a c

Abstract

Colchicine causes both muscle and peripheral nerve toxicity of subacute onset in patients with renal insufficiency. We report three cardiac transplant recipients, treated with colchicine for cyclosporin A (CyA)-induced gout, who developed acute weakness due to colchicine myoneuropathy. The onset of disabling weakness occurred over a 1–2 week period. All three patients had concomitant renal insufficiency and an elevated serum creatine kinase and two had elevated CyA levels at the time of presentation. Electromyography revealed features of myopathy and motor axonal neuropathy in all three patients. Two underwent muscle biopsy which confirmed the presence of sarcoplasmic vacuoles characteristic of colchicine-induced myopathy. All patients rapidly improved with either colchicine dose reduction or drug discontinuation. In conclusion, cardiac transplant recipients treated with CyA and colchicine may be at increased risk of developing colchicine-induced myoneuropathy especially in the setting of concurrent renal insufficiency. In patients with post-transplantation gouty arthritis, other treatment modalities are suggested; and if colchicine is administered, the dose should be reduced, CyA levels should be monitored closely and patients should be assessed for signs of neuromuscular toxicity.

Dehneh et al. Journal of Medical Case Reports (2022) 16:371
https://doi.org/10.1186/s13256-022-03609-y

Journal of
Medical Case Reports

CASE REPORT Open Access

Syrian females with congenital adrenal hyperplasia: a case series

Nada Dehneh[1*], Rami Jarjour[2,3], Sahar Idelbi[4], Assad Alibrahem[4,5] and Sahar Al Fahoum[1]

Abstract

Background: One of the most common types of congenital adrenal hyperplasia is an autosomal recessive disorder with 21-hydroxylase deficiency. The classical form, defined by cortisol insufficiency, is accompanied by prenatal androgen excess causing variable masculinization degrees of external genitalia in babies with a 46, XX karyotype.

Cases presentation: These five case reports highlight the management of Syrian females aged between 0 and 32 years with congenital adrenal hyperplasia. Two of the patients have been raised as males, while two had reconstructive surgery and one had hormonal therapy. Becoming mother was achieved by two patients

Conclusion: The integrated treatment of females with classical congenital adrenal hyperplasia CAH, which includes appropriate surgical procedures and controlled hormonal therapy, gives these females the opportunity to live as they are, and perhaps as mothers in the future.

Keywords: Congenital adrenal hyperplasia, Syria, Case report

Case-series:
Clinical case series

- A case-series is, effectively, a register of cases.
- Analyse cases together to learn about the disease.
- Clinical case-series are of value in epidemiology for:
  - Studying symptoms and signs
  - Creating case definitions
  - Clinical education, audit and research

Case series:
Natural history and spectrum

- **Helps professionals can build up a picture of the natural history of a disease**

Case series:
Natural history and spectrum

- **Population case-series is a systematic extension of this series but which includes additional cases, e.g. those dying without being seen by the clinicians.**

- **Add breadth to the understanding of the spectrum and natural history of disease.**

Case series: Limitations

Usually we cannot estimate the prevalence or incidence rate

- **Breast cancer registry in Jordan: We cannot provide prevalence rates without:**

1. **Population size**
2. **Time- period of data collection**
3. **All cases of breast cancer are registered**

Exception for calculation of the incidence: Jordan National Cancer registry can generate data on the incidence.

All cancer cases in Jordan are reported to the Registry office.

No control group for comparison

Disease registry:
Definition of Registry

- The term *registry* is defined both as the act of recording or registering and as the record or entry itself.

- Therefore, “registries” can refer to both programs that collect and store data and the records that are so created.
- **Special form of case series**

Webster's English Dictionary. [August 12, 2012]. http://www.m-w.com.

Disease Registry

- Patient registries have been defined as:

"an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose(s)."

https://patientregistry.ahrq.gov.

Real World Evidence Analysis

- Customized Real World Evidence Analysis: Application and treatment results of various drugs in clinical routine

- **REAL WORLD EVIDENCE** Analysis – Analysis of defined patient cohorts under “real life” conditions (including all comorbidities, AEs & SAEs incl.)

Types of Registries

- Mortality registry
  - An important thing to know about your patients
- Research Patient Registry
  - Clinical Trials
- Disease or Condition Registries
  - Disease or condition registries use the state of a particular disease or condition as the inclusion criterion.
  - One disease or group of diseases: Cancer registry, multiple sclerosis registry, bleeding disorders.
- Service, intervention, device registry

BMT registry, Biosimilars registry

Uses for Patient Registries

- To observe the course of disease
- To understand variations in treatment and outcomes
- To examine factors that influence prognosis and quality of life
- To describe care patterns, including appropriateness of care and disparities in the delivery of care
- To assess effectiveness
- To monitor safety

Components of disease registry

- Personal Domain
- Exposure Domain
- Outcomes Domain

Ecological studies

Are studies in which information on the characteristics and/or exposures of individual members of the population groups are generally not obtained. Existing statistics are used to compare the mortality or morbidity experience of one or more populations with some overall index exposure. care is needed to avoid the 'ecological fallacy' where inappropriate conclusions are made from ecologic data

Ecological studies

- These studies are used to describe disease or drug use problems in relation to some factor of interest.

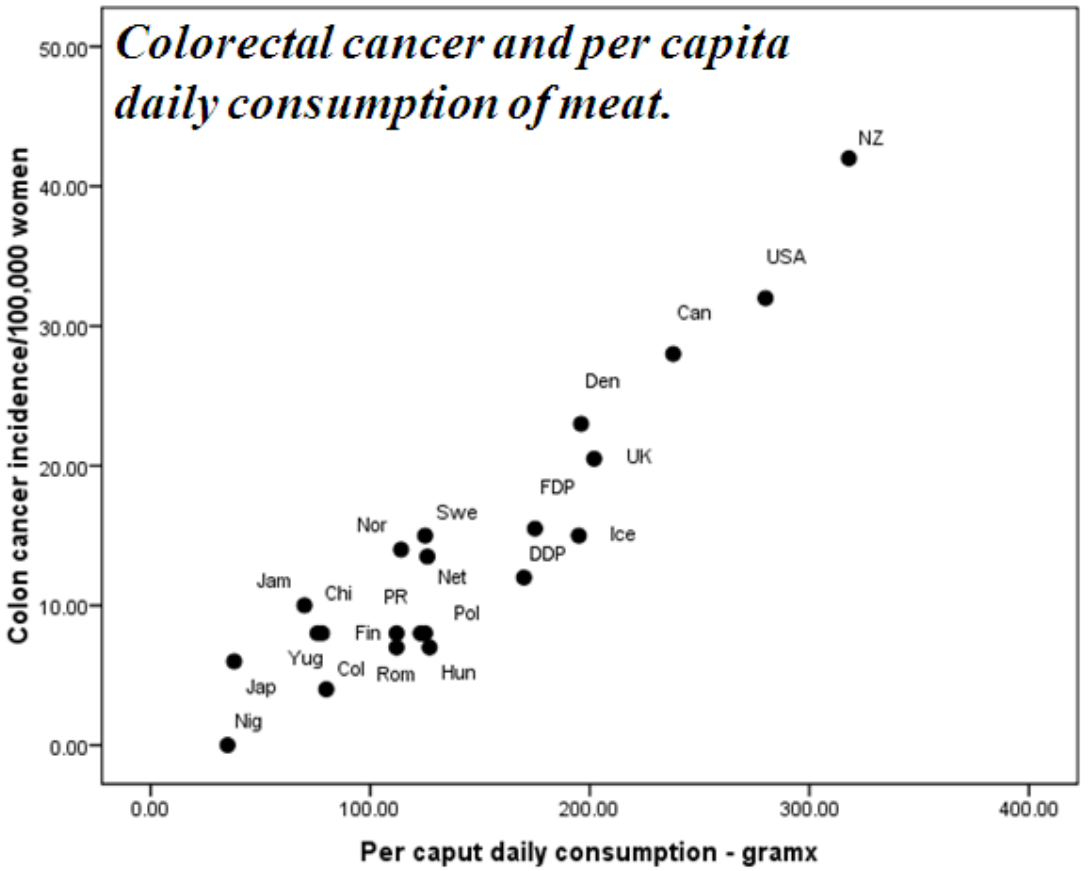
Comparing cigarette consumption with rates of cancer

Comparing Alcohol consumption with coronary heart disease mortality

- Ecological studies are the first identified strong relationships between disease and behavior.

Ecological studies

- In ecological studies the unit of analysis is some aggregate individuals rather than individual persons
- Geographic areas or time period are often used as a basis for defining aggregates
- The analysis centers on determining whether the ecological units with a high frequency of exposure are also unit with a high frequency of disease (+ve correlation) or a low frequency of disease (- ve correlation)



Adapted from: *Int. J. Cancer 15:617, 1973*

Ecological (correlational studies)

- look for associations between exposures and outcomes in populations rather than in individuals.
- They use data that has already been collected.

- The measure of association between exposure and outcome is the correlation coefficent *r*.
- This is a measure of how linear the relationship is between the exposure and outcome variables. (Note that correational is a specific form of association and requires two continuous variables)

Ecological (correlational studies)

Advantages of an ecological study

1. An ecological study is quick and cheap to conduct.
2. It can generate new hypotheses.
3. It can identify new risk factors.

Ecological (Correlational studies)

Disadvantages:

1. It is unable to control for confounding factors. This is often referred to as 'ecological fallacy', where two variables seem to be correlated but their relationship is in fact affected by cofounding factor(s).
2. It cannot link exposure with disease in individuals as those with disease may not be expose.
3. Its use of average exposure levels masks more complicated relationships with disease.
4. Its units of study are populations not individuals. Therefore, the disease rates linked with population characteristics and the association observed at group level does not reflect association at individual level.

CROSS-SECTIONAL STUDY DESIGN

- **Sometimes called *prevalence studies*.**
- **They are studies of total populations or population groups in which information is collected about the present and past characteristics, behaviors, or experiences of individuals.**
- **There are a number of advantages in performing a cross-sectional study.**

- **These studies involve a single data collection and, thus, are less expensive and more expedient to conduct.**

Cross-sectional (or prevalence) studies

Are studies in which a defined population is surveyed and their disease or exposure status determined at one point in time

- **The prevalence rates of disease in the whole population as well as in those with and without the exposure under investigation can be determined**

- **Cross-sectional studies are generally not suitable for a disease which is rare or of short duration as few people will have the disease at any one point in time**

CROSS-SECTIONAL STUDY DESIGN

- **Emphasis is on differences between groups at one point in time.**
- **They provide a one-time glimpse at the study population, showing the relative distribution of conditions, diseases, and injuries—and their attributes—in a group or population.**
- **Point prevalence versus Period prevalence**

Cross-sectional studies

- More effective in identifying chronic diseases and problems
- Less effective in identifying communicable diseases of short incubation periods and short durations.

Cross-sectional (or prevalence) studies

- It is often difficult to separate cause and effect as the measurement of exposure and disease at any one point in time

- Because of this limitation, cross-sectional studies are useful when investigating exposures which do not change e.g genetic characteristics such as ABO blood group and HLA

- Cross-sectional studies are often used as an initial exploration of a hypothesis prior to conducting a case-control or follow-up study

CROSS-SECTIONAL STUDY DESIGN

- **They provide information and data useful for the planning of health services and medical programs.**
- **Assessment of the burden of diseases or healthcare programs leads to setting priorities at the organization, local or national levels.**
- **They are based on a sample of the whole population and do not rely on individuals presenting themselves for medical treatment**

CROSS-SECTIONAL STUDY DESIGN

- Sample size:

1. Question or primary & secondary outcomes
2. Population size
3. Prevalence of condition of interest in the population
4. Distribution of the condition (for example hypothyroidism is common among women age 50 to 70 but less common amongst men at this age group).

   Therefore we need a large sample from men in the general population to get men with hypothyroidism. In this case we stratify for gender.

Cross-sectional study

- Exposure and outcome are assessed simultaneously among individuals in a defined population, thus at one point in time
- No sampling of individuals based on a exposure or an outcome

Two by two table

Exposure	**Outcome**		Total
	Yes	No	
Yes	a	b	a + b
No	c	d	c + d
Total	a + c	b + d	a + b + c + d

Prevalence of outcome in exposed = a / a + b

Prevalence of outcome in non-exposed = c / c + d

Prevalence Rate Ratio (PRR) = $\dfrac{a / a + b}{c / c + d}$

Cross-sectional study

Prevalence of and Factors Associated With Persistent Pain Following Breast Cancer Surgery

JAMA. 2009;302(18):1985-1992

Objective To examine prevalence of and factors associated with persistent pain after surgical treatment for breast cancer.

Design, Setting, and Patients A nationwide cross-sectional questionnaire study of 3754 women aged 18 to 70 years who received surgery and adjuvant therapy (if indicated) for primary breast cancer in Denmark between January 1, 2005, and December 31, 2006. A study questionnaire was sent to the women between January and April 2008.

Cross-sectional study

Chemotherapy	Outcome		Total
	With pain	Without pain	
Yes	664	556	1220
No	879	1088	1967
Total	1543	1644	3187

Prevalence of pain among chemotherapy = 664/ 1220 = 54.4%

Prevalence of pain among no chemotherapy = 879 / 1967 = 44.7%

Prevalence Rate Ratio (PRR) = = 54.4 / 44.7 = 1.22

Cross-sectional survey of CHD among male by physical activity

	Number examined	Number with CHD	prevalence
Not physically active	**89**	**14**	**157.2/1000**
Physically active	**90**	**3**	**33.3/1000**

Cross-sectional studies: advantages

- **Relatively quick**
- **Data on all variables is only collected once.**
- **Sample size depends on the question**
- **Standard measures used**
- **Prevalence estimated**
- **The prevalence of disease or other health related characteristics are important in public health for assessing the burden of disease in a specified population and in planning and allocating health resources.**
- **Good for descriptive analyses and for generating hypotheses**

Cross-sectional studies

Disadvantages:

- They cannot show cause–effect relationships.

Difficult to determine whether the outcome followed exposure in time or exposure resulted from the outcome.

- If the sample is not representative, results are representative only of the individuals who participate in the study

Example prevalence of sickle cell anaemia in the Easter region of the KSA does not represent the who country.

- Not suitable for studying rare diseases or diseases with a short duration.
- Unable to measure incidence
- Associations identified may be difficult to interpret.
- Susceptible to bias due to low response and misclassification