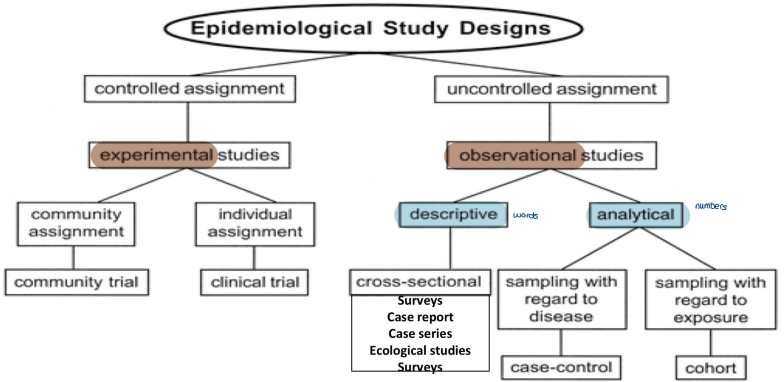


Source: Waning B, Montagne M: *Pharmacoepidemiology: Principles and Practice*: http://www.accesspharmacy.com

According to time

Study design	Method	Advantages	Limitations	notes
Prospective	-we follow people with a certain **risk factor** to see whether they develop a specific outcome or not. -measures of association between factor & outcome must be high enough to conclude a meaningful relationship. -fixed=factor Wide range = outcome	-fewer potential of bias and confounding factors than in retrospective. **-higher reliability of data**.	-**expensive**. -**time** consuming. -**difficult** to access subjects. -loss of subjects from the study over time may be substantial. (**drop out bias**).	
Retrospective	-we study the history of people with an outcome to see whether a specific factor could have caused their **outcome**. -fixed=outcome Wide range= factor	-**inexpensive** -**quick** -**easy** to access a large number of subjects in interest. -useful to study exposure that **no longer occur**. -useful to study **rare outcomes.**	-confounding factors and bias more common. -subjects may not remember past information. (**recall bias**)	
Case report	-a detailed report by a clinician on a single **patient with unusual features** that could lead to a **hypothesis**. -the most common descriptive study.	-starting point of many researches by raising a research question.		-clinical investigators can use **challenge-rechallenge** data to help establish causality or relationship between the unusual feature and a specific factor.

Descriptive

Discriptive

Case series	-a detailed report by a clinician on a **group of patients** with unusual features that could lead to a **hypothesis**.	-recognizing a clustering of similar cases could emergence a new disease or **epidemic**. -helps learning more about a disease **symptoms**, signs. -helps creating case definitions. -useful for clinical education.	-cant provide a relationship between **factor/outcome**. (more concerned with the symptoms) -can't provide **prevalence / incidence** rates (no pop. / not all cases registered). -no control group for comparison.	-**population case series**: An extension of case series study + including additional cases that died without being seen by a clinician. Adv: Understanding the spectrum & **natural history** of the disease.
Ecological studies **(AKA correlational … because the relationship is described as a positive or negative or no correlation)**	-existing statistics about **populations** –usually from different geographic areas or time periods- are used to compare mortality & morbidity taking in consideration the average risk factor in the population (not individuals).	-provide strong relationship between **disease and behavior.** -**quick & cheap**. -generates **new hypothesis.** -can identify new risk factors (as a hypothesis)	-unable to control for confounding factors (**ecological fallacy**). - it doesn't reflect association at individual level. (a case in a population with high average of an exposure may not be exposed.) -don't provide **incidence/prevalence** .	-measure of association used = correlation **coefficient r** … which describes how linear the relationship between the exposure & outcome is.
Cross sectional (AKA prevalence)	-studies in which a population is **surveyed** and their disease & exposure are determined at **the same point of time**. -provides a one-time glimpse at the population, Showing relative distribution of conditions, diseases...	- **inexpensive**. -**quick.** -sample size depends on the question. -provides **prevalence**. -effective in identifying **chronic diseases**. -provide useful information for the planning of health services and **medical programs.**	-not suitable for **rare diseases**. -not suitable for **short duration diseases** (not realistic prevalence). -often difficult to show **cause_effect** relationships as they are measured at one point of time.(ما بنعرف مين السبب و مين النتيجة) -**bias** chance (not representative sample /low response /misclassification) -unable to measure **incidence**. -results may be difficult to interpret.	-often used as initial exploration / generation of a **hypothesis** that is followed by another analytical study (e.g. case control)

Analytical

Case control	-a **comparison** between a group of cases (with one specific disease) and controls (from the same population/as similar as possible) to **determine the factors** that could be responsible for the development/prevention of the disease. -most common among analytical studies. -selection of subjects based on disease status.	-**quick** **-inexpensive** -able to study a wide range of exposures. -able to study diseases with **long latency period**. -can study **rare diseases**. -small sample size is required (compared with cohort)	-not suitable to study **rare exposure** (cohort is better). -cant provide **incidence/prevalence.** -susceptible to **bias** (selection and recall). **-**we cant be certain that the exposure came before the disease. (**factor _ outcome relationship)** -choice of controls may be difficult or not representative. -no absolute risk estimates.	-suitable measure of association = **odds ratio** -methods of data collection : 1.case_note review (ملفات المرضى) 2.postal questionnaire 3.interview (for detailed information)
Cohort	-a **comparison** between a group of exposed & nonexposed people to a specific factor (for a long period) to **determine whether an outcome** incidence of is greater in any of the groups. =selection of subjects based on exposure.	-best study to establish **cause_ effect** relationships. -takes into account seasonal **variation**/ fluctuations & other changes over a long period of time. -provides **incidence and prevalence.** -provides a time related sequence between exposure & outcome. -suitable to study **rare exposures.** -able to study a wide range of outcomes for a single exposure. -**less bias** potential.	-**expensive.** **-time consuming**. -not efficient for **rare diseases**. -needs large samples. -**bias** potentials: -drop_ out bias (seriously affects validity) -changes among diagnostic methods, exposures or study population. -**difficult** (locating subjects, tracking and testing them over a long period).	-examples: -life expectancy of cerebral palsy children. -aspirin intake and colorectal cancer. -purpose (2 dimensions): 1.descriptive (measures frequency). e.g. incidence rates / natural history of the disease. 2.analytic (measures association) e.g. relative risk. Suitable measure of association= **relative risk**.

Retrospective cohort	-we use information about already exposed and diseased people … without having a control group. -all the process is in the past.	-**inexpensive.** **-quick**. -feasible for studying effects for exposures that **no longer occur** (e.g. banned drug)	-relies on existing records (which might not be enough). -relies on subject recall (recall **bias**).	Key difference between retrospective cohort & case control is that we don't have a control group in the cohort.
Ambidirectional cohort	Data collected both **retrospectively and prospectively** on the same cohort to study short and long term effect of exposure.			
Experimental	**-what is it?** Studies of the **effect** of a specific treatment (drug/surgery/new service/type of management) **on patients** with a specific disease to evaluate its efficacy.	**-why do we need it?** -Theory is not enough and have caused previous disasters. -Observational studies show the **correlation** between factors and outcome, but do not ensure **causation**. (evidence: many false positive observational studies e.g. relationship between red meat and breast cancer) + they might not overcome bias and confounding. **SO WE NEED EXPERIMENTAL TRIALS TO ENSURE CAUSALITY, SAFETY & EFFICIENCY.**	-depends on the study type.	-could be clinical/ preventive. -clinical trials could be: Randomized, nonrandomized, single center, multi center, 4 phases trials. -choice of the clinical study design depends on: 1.research question. 2.research goals. 3.researcher beliefs, values & skills. -time & funding. -types of study outcomes: 1.death. 2.clinical measurement. 3.symptoms. 4.quality of life. 5.psychological wellbeing.

Experimental

Randomized clinical trial (RCT)	**-differences from observational:** 1.exposure = manipulated. 2.subjects= chosen by random allocation (whether to be in the experiment or control group). **-mechanism?** Experiment group are given the agent being tested … control group are either given a current drug or a placebo (if there is no current drug). Both patients and investigator are blind to the treatment given to reduce bias (double blinded).	**WE NEED EXPERIMENTAL TRIALS TO ENSURE CAUSALITY, SAFETY & EFFICIENCY.**	-**expensive** -large trials (may affect statistical power). -long term follow up (**drop out bias**). -compliance. -possible **ethical** questions. -patients may make some **sacrifice** (because it requires scientific treatment rather than medical).	-could be single /double/ triple blinded.
Preventive	-studies of the effect of a possible preventive measure on people who **don't have a disease**. -we have an experiment group vs. a control group.	-suitable to find a prevention of **extremely common/ extremely severe** diseases. -suitable to study people who are at high risk of a disease but haven't developed it yet.(e.g. hepatitis B)	**-more expensive**. (the risk of developing diseases is small… which allows a greater number of subjects than clinical trials do = more expensive)	-some studies have to be applied on communities rather than individuals e.g. water fluoridation to prevent dental caries.

Preventive medicine

- what is it ?
- Actions aimed to:
  - eradicate
  - eliminate
  - Minimize the impact of disease or disability
  - If non of the above is feasible ... Retard the progress of it.

Medical Screening

What is it ?

the systematic application of a test for people who haven't sought medical attention on account of symptoms of disorder, to identify who are at risk of developing that disorder

- Further investigation
- Direct preventive action

Aims

- for individuals :-
  - Better prognosis /outcomes
  - e.g. Medical screening of breast cancer decreased mortality in England & Wales
- for community
  - Protection from communicable diseases
  - Rational allocation of resources
  - Mortality ↓
  - quality of life ↑
- for medical field
  - Research (understanding natural history of disease.)

Types of medical screening according to Subject

- Random Screening (e.g. pink october)
- Opportunistic Screening [case finding]
  - Subjects = people who seek health care for another reason
    - check lipid profile for overweight patients
    - refer women > 40 years to breast cancer screening

Screening vs Diagnosis

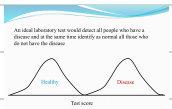
- Screening assists in early diagnosis of signs / symptoms
  - At GPs & selected specialists.
  - general population awareness.

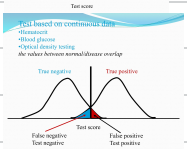
Screening Criteria

- Disease should be an important health problem
  - well defined, known epidemiology, natural history, prevalence
  - common / serious - Even if not highly prevalent.
    - Neonatal screening for inborn metabolism errors.
    - Phenylketonuria ~ early detection prevents severe impact only by dietry restriction.
    - Hypothyroidism
- Presence of pre-symptomatic or early stage of the disease
  - to ensure ... we do RCT to see if there is a difference between early detected Patients (By Screening) and people who seek health care after symptoms
- Screen for the disease not the risk factor

Screening test

- Should be :-
  - Safe
    - No, minimal adverse effects (e.g. pain)
  - Inexpensive
  - Acceptable
    - considering convenience & test duration
  - valid & reliable





Sensitivity (Detection rate) = $\frac{TP}{TP+FN}$

Specificity = $\frac{TN}{TN+FP}$

- False positive rate = $\frac{FP}{FP+TN}$ = 1-Spec

Why important ?

- we need to make it as low as possible ... to avoid :-
  1) Affecting the economic by further investigations.
  2) psychological distress.

- Predictive values :-
  1) Positive predictive = $\frac{TP}{TP+FP}$
     - How likely it is to have the disease when the test is positive
  2) Negative predictive = $\frac{TN}{TN+FN}$
     - How likely it is to be healthy when the test is negative
- Prevalence = $\frac{TP+FN}{All}$

Validity of tests

Reliability means that the same results should be obtained by different observer or the same observer at different occasions

Post - Screening process

- Agreed plan on further investigation, diagnosis & treatment

Agreed plan on further investigation, diagnosis and treatment:

- Where to refer your positive subjects
- What is the diagnostic tests
- Who will pay for the investigations and treatments
- Diagnostic tools, screening intervals and treatment
- Facilities required for such steps should also be available or easily installed and equally accessed by the screened population

How to make Screening project more efficient ?

1) Do it Systematic - instead of scattered campaigns & activities.
   - How? obtain data about residents in a specific area - Arrange GP visits for them
2) Make it Simple
   - cut it down so it will be simple
3) test it before you generalize it

Test it before you generalize it

- Start with pilot program
- Assess response rate
- Is my program cost-effective
- What is my cost-effective screening criteria
- Quality of all involved steps (single versus double reader mammography screening, FIT versus Haemoccult test)
- Compare respondents with non-respondents
- Assess success rates
- Look for determinants of success and failure
- Is there a specific group who needs different intervention?

why do we need a pilot project

Importance of Pilot Projects

1. Health economics evaluation
2. Setting age cut-off based on local data
3. Improve performance at national level by learning from experience at pilot phase
4. Comprehensive assessment of the screening program helpline, waiting time, film quality, guidelines such as double readers, false positive rate, false negative rate, diagnosis process, psychological counseling, treatment, prognosis, economic evaluation, how can we make it better at the national level.
5. Assessment of barriers to screening
6. Quality assessment of staff

- Acceptability to the public & health care staff.
  - Screening, Diagnosis, therapy should be ethicaly accepted.
- Economic evaluation
  - Screening test must save money of disease treatment.
    - to ensure that :
      - Choose the correct disease to screen.
      - Choose the correct group at risk to screen.

Economic evaluation:

- Implementing screening programmes should be more economically effective than the existing system.
- Cost of all steps related to the screening programme should be assessed and compared with outcomes of the screening and with other services.
- **Each country should has its own studies and data**
- What is cost effective in the UK might not be cost effective in Jordan or India
- In breast cancer screening: age range for screening plays a key role in the cost-effectiveness of the program
- UK (Screening aged 50-70 Every three years, then in few years ago aged 40-49 at high risk)
- Sweden (age 40-70) annually

- Bias related to medical screening

1) lead time Bias ~ detecting the disease earlier **Appears** to prolong the survival time, but it doesn't because early treatment is actually not better. e.g. prostate cancer
2) length time Bias ~ the cases more likely to be detected by routine screening are usually slowly progressive & might not harm the patient in lifetime. + this is a Form of Selection Bias
3) Selection Bias ~ Responders are different from decliners.
4) Volunteer Bias ~ Related to point 3 & more common among nonsystematic screening

Quality Assurance

- Quality assurance means that the assessment of the service provided and applying modifications when necessary.
- This includes various steps such as recruitment, registration, waiting time, test procedures, results handling and follow up or referral for treatment procedures.
- Clinical audit

- After all steps of pilot studies & Quality Assurance your program will be in place.
- Now, you need to continue monitoring and regular evaluation.

لما اشتد الحصار على المسلمين في
المدينة ، وأنهكهم التعب ، قام الرسول
صلى الله عليه وسلم الليل ودعا :

اللهم منزل الكتاب ، سريع الحساب
هازم الأحزاب ، زلزل الأرض
تحت أقدامهم .