MAKERERE UNIVERSITY SCHOOL OF PUBLIC HEALTH

MPH 7102: APPLIED EPIDEMIOLOGY I

Coordinating Department
Epidemiology and Biostatistics

Master of Public Health
Distance Education Programme

COURSE MATERIALS

4th Edition
(May 2019)

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Makerere University School of Public Health

Edition 4

(May 2019)

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Makerere University School of Public Health
Master of Public Health – Distance Education Programme

1.0 ABOUT THIS COURSE

1.1 COURSE TITTLE: Applied Epidemiology I

Course Code: **MPH 7102**
Credit Units: **3**
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1.2 GENERAL OUTLINE OF THE COURSE

This course will cover the following areas:

Unit 1: Introduction to Epidemiology
Unit 2: Descriptive Epidemiology
Unit 3: Analytical Epidemiology
Unit 4: Interventional Epidemiology

1.3 INTRODUCTION

Welcome message from the Course Coordinator: As coordinator for applied epidemiology, I wish to welcome you to this exciting discipline of epidemiology. Epidemiology is one of the courses that form the backbone of Public Health. As you will learn, epidemiology has evolved over the last 150 years into an important discipline in the health sciences, cutting across different scientific fields and disciplines. Epidemiological principles are cut across all disciplines in public health. This is a course you ought to master, in order to have good grounding for other course units in your MPH program.

About this course: This course introduces you to the principles, concepts and terms used in epidemiology and their application in public health. Epidemiology is a core discipline of public health. The course takes a practical approach, translating theory and concepts into everyday problems and challenges faced in public health practice and especially in appreciating the distribution and determinants of disease and health related states. It defines the epidemiological approach to interrogation of disease and health related events, so as to understand the factors associated with these events.

Contributors and Resource persons: I wish to extend sincere thanks to all the facilitators for this course for their time and dedication during the development of the course materials. The facilitators are: Dr. Victoria Nankabirwa, Dr. Joan Mutyoba, Prof. Fred Wabwire-Mangen, Dr. Edith Nakku-Joloba, Dr. Barbara Kirunda, and Dr. Mayega Roy William. If you have any specific problems related to this course, feel free to contact the course coordinator for guidance and support [Email: vnankabirwa@musph.ac.ug].

The Course Coordinator

Dr. Victoria Nankabirwa	

The Instructional Designer: Roy William Mayega coordinates the improvement and enhancement of the learning materials. Specific issues related to the content and design of the materials may be routed to him on the address de_materials@musph.ac.ug.

1.4 COURSE AIMS AND INSTRUCTIONAL GOALS

1.4.1 Aim

The overall aim of this course is to provide the student with the knowledge and skills to apply the basic epidemiological principles and concepts in determining the distribution and determinants of health-related states, and the use of this information in the control of disease.

1.4.2 Instructional Goals

By the end of this course, the MPHO should be able to:

- Illustrate the principal epidemiological concepts and their roles within the health system, especially in the detection, measurement and control of disease
- Use appropriate calculations to quantify public health events and validate methods
- Design, conduct and analyse observational epidemiological studies that are descriptive or analytical in nature
- Evaluate the principle concepts of epidemiological interventions, and apply them to disease prevention and control

1.5 TIME FRAME

You will cover this course during the first semester of the MPH Distance Education Program. The semester runs for a total of 15 weeks including time for front loaded lectures and examinations.

1.6 INSTRUCTIONAL MEDIA AND TECHNIQUES

1. **Orientation Session:** Brief instructor led face-to-face orientation sessions will be delivered at the School of Public Health at the beginning of the course. The purpose of the sessions is to give you an overview of what you are expected to read about, and guide you on the resources available.
2. **Print material:** You will be provided with handouts of print materials (MUIPH Distance Education Resource Kit) and other materials. You will also be provided with printed case studies where necessary. There is an additional resources kit containing a collection of handouts and readers that have been sorted for you. You will be expected to acquire this at your own cost. We highly recommend that you get yourself a copy of this kit. Copies are available at the Business Centre at the going rate for photocopying services in the school.
3. **E-mail:** E-mail shall be the main means of communication for submission of assignments, announcements and consultation with faculty. Please ensure that you obtain a reliable e-mail

address and register it with the Programme Administrative Secretary. In case you change your e-mail, please promptly notify the same officer.

4. **E-Learning Platforms and Tools:** Learning Management tools shall be used to conduct online discussion forums and chatting. You will be informed in due course about the site to be used for hosting these interactive activities.
5. **Textbooks, internet and independent study:** You are required to search for the relevant references and acquire the core recommended readings for each course. There are also many internet sources from which you can obtain information.
6. **Activities, examples and exercises:** Please note that the biostatistics course involves a lot of calculations. It is important, especially, that you do all the exercises and examples given, so that you internalize the application of the statistical methods they convey.

1.7 MODE OF EVALUATION

1.7.1 Progressive Assessment – Self Assessment

Self-evaluation: You will be required to attempt a set of exercises and questions at the end of each presentation for your own assessment. Assignments and activities in the course are for you to test yourself and evaluate your performance. They will enable you gauge your understanding of the content. Answers to these questions may be availed in the Additional Resources section of this document. You will also be required from time to time to contribute to specific discussion points that have been set up for analysis on the discussion forums.

Participation: We may also request you to contribute to the topics put up on the discussion boards and your contribution may be graded. Your active participation in the discussion boards and the posted assignments may contribute to your progressive mark.

1.7.2 Progressive Assessment – Hand-in Assignments/Tests

In line with the University regulations, you will be evaluated in two segments; progressive assessment, which accounts for 30% of the total mark and the end of semester university examination which accounts for the remaining 70%. Apart from the self-assessment exercises, the School shall require you to hand in one or more assignments for marking. These assignments may be in form of quizzes, structured questionnaires, long or short answer questions, term papers or project reports, to be forwarded on-line. An assignment for assessment will be indicated and will either be given to you at the time of the face-to-face, or forwarded to you by registered mail or internet. Please pay close attention to the deadlines for handing in the assignments. Progressive assessment will account for 30% of the overall course score.

TAKE NOTE THAT THE PROGRESSIVE ASSESSMENT IS A PRE-REQUISITE FOR YOU TO SIT THE END OF SEMESTER EXAMINATION.

1.7.3 University Exam

You will sit for a final course examination at the end of the semester to be held at the Institute of Public Health. You must make arrangements to travel to the Institute for this examination once the date has been communicated to you. This will contribute about 70% of the final mark

1.8. EVALUATION OF THE INSTRUCTION PROCESS

1.8.1 PRE AND POST EVALUATION

NOTE: Before using these materials, you are kindly requested to fill the ***Evaluation Questionnaire*** for this semester and send it to the **Instructional Designer**. This questionnaire is not a test, but it

will enable us to measure your expectations from the instruction process and to gauge how much you will benefit from the instruction materials for this semester, as well as inform us the extent to which the materials given in the previous semester assisted you. The questionnaire has two parts: **A Post Evaluation** of the previous materials and a **Pre-evaluation** of the materials that you expect in the new semester. In the post evaluation section, you are requested to evaluate the materials that you received in the last semester. In the pre-evaluation section, you are expected to inform us of the key competencies and qualities you expect from the new materials. Your responses will be compared with responses in the ***Post evaluation section*** *at the beginning of the next semester.* The information generated will be used in an iterative process designed to improve the materials. This evaluation may be administered during the face-to-face session, before the materials are dispatched. In the event that it is not delivered then, you can access it in your Additional Resources Folder. In case you do not fill it during the Face-to-face sessions but fill it later, you are requested to send the completed questionnaire to the Instructional Designer at the e-mail address: de_materials@musph.ac.ug.

1.8.2 PRETEST

NOTE: It is important that before you read these materials, you complete a **Pre-test**. The purpose of this test is to make a baseline assessment of what current knowledge you have. It is also an important guide to what areas you need to emphasise in your reading. For some courses, where the Course Coordinator considers it a requirement, the test may be administered at the time of face-to-face, during the introduction to this course. Otherwise for other courses, it is strictly **optional**, but you are encouraged to take it prior to your reading. The test is also contained in the **Additional Resources Folder**.

2.0 COURSE CONTENT

2.1 Unit 1: INTRODUCTION TO EPIDEMIOLOGY

2.1.1 Introduction to the Unit

Disease is not randomly distributed in populations; rather, there are factors that determine and therefore influence the predisposition and distribution of disease in a particular population. Epidemiology therefore focuses on the determinants of disease or health related events in a population. This module introduces the learner to the definition of Epidemiology, the historical perspectives and milestones in the development of epidemiological thinking and the emergence of epidemiological methods as well as key concepts in the subject of Epidemiology. It outlines the importance of Epidemiology in health service delivery systems.

2.1.2 Unit Outline

The following topics will be covered:

- Introduction to Epidemiology
- Historical Perspectives
- Key Concepts in Epidemiology
- Uses of Epidemiology

2.1.3 Instructional goal

The MPHO should be able to illustrate the principal epidemiological concepts and their roles within the health system, especially in the detection, measurement and control of disease

2.1.4 Unit Objectives

By the end of this unit, the student should be able to:

1. Define Epidemiology
2. Illustrate, with examples, the key historical milestones in the development of epidemiological thinking
3. Relate the key epidemiological concepts to public health events
4. Demonstrate the uses of Epidemiology in the management of health events

2.1.5 Time Frame

1 WEEK

2.1.6 Content

Lesson 1: Introduction to Epidemiology

Lesson Topics:

a. *Background information and Definition of Epidemiology*
b. *Classification of Epidemiology/Applied Epidemiology*
c. *Historical Perspectives in Epidemiology*
d. *Key Epidemiological concepts*
e. *Uses of Epidemiology*

Lesson Objectives:

By the end of this lesson, the MPHO should be able to:

1. Define Epidemiology
2. Illustrate, with examples, the key historical milestones in the development of epidemiological thinking
3. Demonstrate the uses of Epidemiology in the management of health events

a. Background information

Definition of Epidemiology: Epidemiology has been generally defined as "*the study of the distribution and determinants of health-related states or events in specified populations and the application of this study to the control of health problems".*

> The term epidemiology has its root in the word "epidemic" a combination of three Greek words, "**epi**" meaning upon, "**demos**" meaning people and **"logos"** meaning knowledge.

Epidemiology is for good reason considered the basic science of public health. Epidemiology is:

a) a quantitative basic science built on a working knowledge of probability statistics, and sound research methods,
b) a method of causal reasoning based on developing and testing hypotheses pertaining to occurrence and prevention of morbidity and mortality; and
c) a tool for public health action to promote and protect the public's health based on science, causal reasoning, and a dose of practical common sense.

There are two fundamental assumptions of epidemiology:

a) First, that human disease does not occur at random, and
b) Secondly, according to Heinekens, human disease has causal and preventive factors that can be identified through systematic investigation

b. Classification of Epidemiology

Epidemiology is broadly categorized into observational and experimental epidemiology. Under observational epidemiology, we have the two main arms of descriptive and analytical epidemiology, while experimental epidemiology is divided further into clinical trials and community trials. We will - cover these in detail later.

Applied Epidemiology: The term "applied epidemiology" is sometimes used to describe the application, practice or use of epidemiology in addressing public health issues and events; examples of applied epidemiology include the following:

a) Monitoring of reports of communicable diseases in the community and defining interventions
b) An investigation of whether a particular dietary component influences the risk of developing cancer
c) Evaluation of the effectiveness and impact of a cholesterol awareness program
d) Analysis of historical trends and current data to project future public health resource needs

c. Historical Perspectives in Epidemiology

Evolution of disease causation theory: The concept of disease causation has gone through several eras and man's thinking has changed over time. For instance, the Greek originated miasmatic theories postulated that disease was caused by climatic changes that affected the population, and local disease outbreaks were due to noxious air (the miasma) that hangs low over the earth. This is demonstrated by the Romans who believed that 'bad air' that mainly lingered around 'swampy' areas' was responsible for 'Malaria' around the Mediterranean region. Lord William Farr also fronted the theory in explaining the outbreak of Cholera in 19th Century London. He postulated that a cloud that hangs low above the earth caused the disease.
John Snow: Snow was an anesthesiologist, who disagreed with the miasmatic theory. By comparing two communities, Snow observed that most cases of Cholera originated from a settlement that was utilizing water from companies that pumped the water down stream from a site that he suspected was contaminated. One company (the Lambeth Company) shifted to a location that was further upstream, whereupon Snow observed that communities that used this water reported fewer cases. Snow used the ''Shoe Leather Epidemiology'' in which he conducted a door-to-door search for cases and deaths, and inquired from which source their water supply was.

Note:
- At the time, there was no knowledge of that germ are the immediate causes of disease
- It was by observation that Snow was able to detect an unusual pattern
- This is the basis if the ''Epidemiological Approach'' – From determining associations between exposure factors and disease, to inferring causality
- A detailed knowledge of microbiology and pathogenesis is not totally required for detection and control of disease; careful observation and investigational skills for underlying factors are equally as important

Edward Jenner (Born 1749): In 18th Century Europe, 400,000 people died of smallpox each year; a third of the survivors were blinded. Edward Jenner observed that cow maids who developed ''cowpox'' a much milder disease than smallpox did not contract small pox – this observation led to development of a vaccine for smallpox. Edward Jenner did not know anything about viruses. He used purely observational data to formulate a hypothesis as the basis for preventive action.

d. Key epidemiological concepts

1. What is the epidemiologist's view of health? Imagine that a sociologist, medical doctor and an economist are asked to design interventions to address a particular health problem; what do you think each one of them will do? The sociologist might focus on the behavior and culture of that community as the important issues, the medical doctor may recommend allopathic therapies, while the economist may think that poverty is the main underlying issue that must be addressed. Epidemiologists recognize that ill health has more than a biomedical dimension. Epidemiology has

evolved to embrace several paradigms of ill health, giving it a holistic outlook to health and ill health. New fields like **Social epidemiology** have emerged with a strong emphasis on the social, cultural and economic domains of health.

2. The Epidemiological Approach: The epidemiological approach is a two-step inquiry about the aetiology of disease or promotion of health-related states. It is a two-step approach:

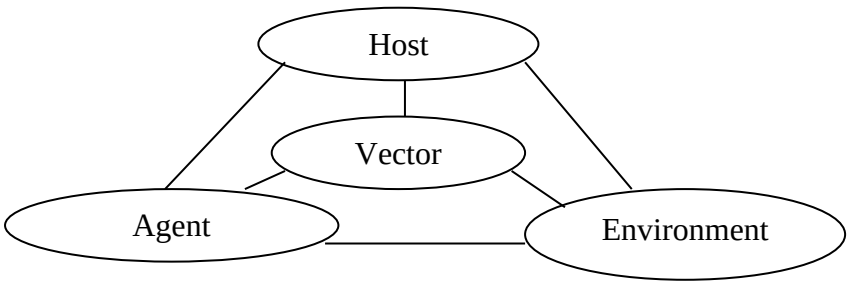
Step 1: Determine association between plausible factors and health related events by studying characteristics of the events in groups and individuals

Step 2: Determine the causal relationship: If there is an association, is it really causal?

Activity 2.1.1: Suggested Reading – Fluoride in water and the control of dental carries
A study was conducted in Newburg and Kingston – New York to determine the association of reduction in dental carries with fluoridation of water. On determining the association, further analysis was done to infer that indeed use of fluoridated water reduces incidence of dental carries [Read: Gordis: Epidemiology; Third Edition; Pages 8-9]

3. The Dynamics of Disease Transmission

The Epidemiological Triad: Human disease arises from an interaction between Host, Agent and Environment. [You were introduced to this concept In Module 1(Biological Basis of Public Health and Introduction to Community)]. The triad is illustrated below:



Mode of Transmission: The modes of disease transmission can be:

Direct: Person to person transmission

Indirect: This involves another conduit, in the transmission process. This could be a 'vehicle' or a vector.

a. Vehicle: Common Vehicle
    i. Single exposure
    ii. Multiple exposures
    iii. Continuous exposure
b. Vector

Immunity: Immunity is either innate (skin, integument or phagocytic cells) or specific (adapted). Specific immunity may be active (following exposure to disease, by infection or vaccination) or passive (passed on either from mother to child or through antibodies) [You were

introduced to this concept In Module 1(Biological Basis of Public Health and Introduction to Community)].

Herd Immunity: It is the resistance of a group or defined population to invasion and spread of an infectious agent, based on the resistance to infection of a high proportion of individual members of the group. The resistance is a product of the number susceptible and the probability that those who are susceptible will come into contact with an infected person. An example is the case of measles vaccination: If 95% of the population in vaccinated and immunized, the remaining 5% of the population is likely to be protected from the disease because it will be difficult for a case of measles to get in contact with another person that is not immunized. Why is this phenomenon important? – When conducting certain mass disease prevention programmes, we may not necessarily cover the entire population. This makes sense because of the limited resources. All that may be needed is to cover a threshold that is necessary to create herd immunity. However, there are certain conditions necessary for ideal herd immunity:

c. The disease agent must be restricted to a single host species in which transmission occurs
d. Transmission should be relatively direct (person to person). Ideally, there should be no reservoir outside humans
e. Assumes random mixing of populations; this is theoretical as most people stay in family/household settings

The proportion of the population required to be immune varies according to the agent, its transmission characteristics, the distribution of immunes and susceptibles, and other (e.g. environmental) factors.

4. Natural history of disease: It is the course of a disease from onset (inception) to resolution. Many diseases have certain well-defined stages that, taken all together, are referred to as the 'natural history of the disease' in question. The stages are as follows:

1. Stage of infection or pathologic onset
2. Pre-symptomatic stage i.e., from onset to the first appearance of symptoms and/or signs. Screening tests may lead to earlier detection.
3. Clinically manifest disease, which may progress inexorably to a fatal termination, be subject to remissions and relapses, or regress spontaneously, leading to recovery. Some diseases have precursors. For example, elevated serum cholesterol is among the precursors of coronary heart disease. Early detection, as by screening, and intervention can alter the natural history of many diseases.
4. Convalescence: The stage in which the disease process resolves, resulting in a return to normalcy.

In general, disease may be preclinical, sub-clinical, latent, and chronic/persistent or a person may remain in a carrier state.

e. Uses of Epidemiology

Activity 2.1.2: Uses of Epidemiology Think about what we have discussed so far and the work of John Snow, and discuss the potential uses of epidemiology. **[This exercise should take you about 20 minutes to complete]**
In your discussion of the uses of epidemiology, you may have been able to raise the following applications of epidemiology: a) Identifying the aetiology of disease and risk factors b) Studying the extent of a health or health problems in a population c) Studying the natural history of disease,

d) Evaluating existing and new preventive and treatment interventions
e) Informing the policy making process.

The applications of Epidemiology

While basic research may add to our biological understanding of why an exposure causes or prevents disease, only epidemiology allows the quantification of the magnitude of the exposure-disease relationship in humans and offers the possibility of altering the risk through intervention. Following are the uses of epidemiology:

1. ***Determine the extent of disease problems in a community:***
   What is the burden of disease in a community? This is an important question for planning.
2. ***Investigate the etiology or cause (s) of a disease and modes of transmission:***
   We want to know how the disease is transmitted from one person to another or from a nonhuman reservoir to a human population. If we can identify the etiologic or causal factors for disease and reduce or eliminate exposure to those factors, we can develop a basis for prevention programs.
3. ***Study the natural history and prognosis of disease:***
   Certain diseases are more severe than others; some may be rapidly lethal, but others may have longer durations of survival. We want to define the baseline natural history of a disease in quantitative terms.
4. ***Evaluate new preventive and therapeutic measures and new modes of health care delivery:***
   Does a new technique or intervention improve survival, quality of life or other health outcomes?
5. ***Provide the foundation for developing public policy and regulatory decisions relating to environmental problems:***
   Which occupations for example are associated with increased risk of disease and what type of regulation is required?

2.1.7 Extension Activities

Extension Activity 1: Discussion Forum Question

With a specific citation, discuss how any one historical milestone is linked to the development of the "Epidemiological Approach".

Extension Activity 2: Self- Assessment Quiz

QUIZ 2.1.1
(Select one correct option)

1. Epidemiology is often defined as: -
    a. An observational science that links factors with health-related states
    b. The use of analytical techniques to study the distribution and determinants of disease
    c. The study of the application of interventions in the control of disease
    d. The action oriented scientific study of the distribution and determinants of disease

2. The Epidemiological Approach is often viewed as a two-step approach. It involves: -
    a. Determining disease associated factors and testing associations to infer causality
    b. Measuring disease occurrence and testing associations to infer causality
    c. Observation of health-related phenomena and describing the unusual patterns there from
    d. Determining causality and designing appropriately targeted interventions

3. Herd immunity is the resistance of an entire population conferred by the fact that a critical proportion of the population is protected. The probability of a susceptible person meeting a diseased person is negligible. The above situation will only hold if the following assumption is true:
    a. That 95% of the population is vaccinated and immunised
    b. That the disease agent is restricted to one single host in which the disease occurs
    c. That transmission is indirect, with an extra-human reservoir
    d. That the population is organised in structured communities with minimal mixing

4. The following are uses of Epidemiology, except: -
    a. Identifying aetiological agents and high-risk groups
    b. Identifying natural history of a disease
    c. Identifying the interventions that are efficacious
    d. Isolating biological agents implicated in disease aetiology

5. One of these statements is true about the disease transmission process
    a. Point source transmission involves the propagation of one agent to several susceptibles
    b. Multiple exposure refers to the continuous uninterrupted contact with a disease-causing agent
    c. Common vehicle transmission involves the propagation of infection from a unity source
    d. The conduit in “direct transmission” is either a vehicle or a vector

2.2 Unit 2: DESCRIPTIVE EPIDEMIOLOGY

2.2.1 Introduction to the Unit

Epidemiological inquiry often begins with descriptive information as the basis for formulating hypotheses on factors associated with a particular disease or health related event. Epidemiologists therefore first observe for abnormal phenomena or events, following which they discern trends that are out of the ordinary. Descriptive epidemiology deals with the basic concepts in describing the health-related events by studying characteristics of the events in groups and individuals. Descriptive does not necessarily involve comparison but rather, provides a succinct description of the phenomena of interest from which epidemiologists are keen to detect abnormal events that may necessitate further analysis. In this unit, we shall discuss some key methods used in descriptive epidemiology.

2.2.2 Unit Outline

The following topics will be studied:

1. Parameters used in the measurement of disease in populations
2. Standardisation of rates
3. Validity and Reliability of measurements
4. Principals of disease surveillance
5. Outbreaks and Outbreak Investigation
6. Descriptive Epidemiological Study designs

2.2.3 Instructional goal

By the end of this unit, the MPH student should be able to use appropriate methods in descriptive epidemiology to quantify public health events in given population

2.2.4 Unit Objectives

By the end of this unit, the MPH student should be able to:

1. Differentiate between incidence and prevalence
2. Explain the use of rates, ratios and proportions to express the level of disease and other health related events in populations
3. Apply standardisation techniques to enable unbiased comparison of rates from two or more non-homogenous populations
4. Evaluate sensitivity, specificity and predictive value of measurements
5. Select appropriate methods for evaluating the reliability of measurements
6. Outline the principles of disease surveillance
7. Conduct and outbreak investigation
8. Design and evaluate cross-sectional studies to describe health related events in populations

2.2.5 Time Frame

2 WEEKS

2.2.6 Content

Session 1: Parameters used in the measurement of disease

Physicist James Maxwell (1831-1879)
"We owe all the great advances in knowledge to those who endeavour to find out how much there is of everything"

Engineer, Mathematician and Physicist Lord Kelvin (1824-1907)
"One's knowledge of Science begins when one can measure what one is speaking about and express it in numbers"

Since epidemiology is about the distribution and determinants of disease or heath events in a population, it is important that disease can be quantified in populations. The epidemiological approach is a two-step process: First we describe phenomena in populations. The extent to which they occur (i.e. their level of occurrence) can tell us if there is an abnormal trend. Thereafter, we set up analytical studies to understand the associated factors. In order to do describe the level of health related events in populations, we need some parameters that can be used to summarise the extent to which these characteristics occur in populations. To measure these parameters however, we have to conduct 'epidemiological studies' (either in form of surveys or by continuous tracking of events using surveillance). Thereafter, we describe disease in populations using these parameters. This section introduces you to the types of parameters used to summarize the level of occurrence of disease and health related events in populations, how they are calculated, and their relevance to public health.

Lesson Topics:

a. Rates, ratios and proportions
b. Measures of Morbidity – Incidence and prevalence
c. Measures of Mortality
d. Other rates/specific rates

Lesson Objectives:

The MPH student should be able to:
1. Differentiate between incidence and prevalence
2. Use rates, ratios and proportions to measure disease and other health related events

a. Ratios, Proportions and Rates

Introduction: The occurrence of diseases or health related events can be measured using surveys or surveillance. Thereafter, we describe the outcomes we have found using certain parameters that summarize the situation in the population. We use rates, ratios and proportions. The three parameters are important in comparing disease or health states in different populations.

Rates tell us how fast a disease or event is occurring in a defined population in a defined time (i.e. how rapidly it is changing).

Proportions tell us the fraction of the population that is affected.

Ratios are values obtained by dividing one quantity by another. They are similar to proportions, except in that the denominator is only used as a reference.

All the three frequency measures above are based on a similar formula:

Ratio, Proportion, Rate = $x/y \times 10^n$

X represents a Numerator while Y represents a Denominator. These two lead to a quotient (i.e. a fraction). 10^n represents a constant while ^{n} is a multiple of 10, and 10^n ranges from 1, 10, 100, 1000, etc.
The constant is necessary to allow removal of decimal points especially where the quotient generates a very small number. The selection of which constant to use depends on how rare the events in the numerator are. Rare events may require larger constants e.g. X100, 000 while more common evens require smaller constants e.g. Percent (%)

Let us start with ratios using the example of variable sex: boys or girls.

Fig 3: Boys and girls

Girls	**Boys**
♀♀♀♀	♂♂♂♂

A ratio: May relate boys to girls in form of x:y i.e. x/y. The numerator x represents boys and denominator (girls) are represented by y. Here, the two events are completely independent. This is the usual situation. But, in some situations x may be part of y in expressing a ratio e.g.
Compare:

Boys / Girls = Ratio x/y shows that x is not part of y

Boys / Boys and girls = Ratio x/y shows that x is part of y.

Both these examples are ratios but the latter shares some characteristics with proportions as we see later. The key issue to note about ratios is that not all items in the denominator are capable or at risk of being part or ''converting'' to the numerator.

The Maternal Mortality Ratio: One of the most widely used ratios is the Maternal Mortality Ratio. It is expressed as the ratio of the number of women who die over a specified period of time from causes related to pregnancy and childbirth for every 100,000 live births. We may ask ourselves why the denominator used is not at all related to the numerator. However, if we were to use all pregnant women, our estimate would have several problems. In developing countries, the diagnosis of pregnancy is difficult in the 1st trimester. There are a lot of miscarriages and illegal abortions that go unreported, either due to recall limitation, lack of information or deliberate concealment. If we were to use this for comparison of countries, the mortality calculated will be much different from the actual. Live births are much easier to document across countries and the MMR is a better tool for comparing maternal mortality between countries or states.

A proportion: This is actually, a special form of ratio in which *x (the numerator)* is included in *y (the denominator)*. Therefore, the second example above is strictly speaking, a proportion. Here, the numerator is always included in the denominator i.e. all persons in the denominator are capable of becoming part of the numerator. However, it differs from a true rate because the numerator includes both **new and existing cases** (prevalent cases)

Proportion = $\frac{\text{No. Of cases (new and existing) in a given period}}{\text{Population at risk in a given time}} \times 10^n$ $(x/y \times 10^n)$

A rate: Like ratios, and proportions, rates are a frequency measurement, which is a proportion with an added element of time, and in which the denominator includes only new cases. Rates measure occurrence of events in a given population over a specified time period. Like in a proportion, all persons in the denominator are at risk of becoming part of the numerator. However, it differs from a proportion because the numerator includes only **new events** (prevalent cases). The formula is denoted as:

Rate = $\frac{\text{No. Of new cases/events in a given time}}{\text{Population at risk in a given time}} \times 10^n$ $(x/y \times 10^n)$

The denominator includes:

(a) The population from which cases in the numerator arose.
(b) The counts in both the numerator and denominator are over the same period of time.
(c) In theory, the persons in the denominator are at "risk" for the cases to develop i.e. there must be a possibility for them to experience the disease/event.

Uses of ratios, proportions and rates: These are used to describe/measure degrees of morbidity, mortality and health related states (e.g. natality (birth), fertility, use of family planning, etc).

Examples:

Morbidity (disease)
→ Ratios used include: risk ratio (relative risk) and odds ratio.
→ Proportions used include: attributable risk/proportion, point prevalence, etc.
→ Rates used include: incidence rate/attack rate, person-time-rate etc.

Mortality (death) mortality ratio. etc.
→ Ratios include: maternal mortality ratio, proportionate/proportional
→ Proportions include: case fatality rate, proportionate mortality, etc.
→ Rates include: crude mortality rate, infant mortalityrate, etc.

Other health events
→ Ratios include: child-woman ratio, low birth weight ratio.
→ Rates include: crude birth rate, crude fertility rate, etc.

It is important that you get yourself acquainted with these measures and how they can be derived from raw data. However, before you delve into the above, please note these points below:

a. In ratios, when we use x/y, x (the events) are not necessarily part of y (the comparator). Y is not necessarily the base population from which x (the events) of persons exposed to a risk for development of x and is not necessarily part of y itself, is not necessarily a population exposed to risk.
b. In proportions, the numerator x is always included in the denominator y; However, time is not a component of this measurement.
c. In rates, like proportions, the numerator x is always part of the denominator y i.e. derived from y, but on top of that, the period of time over which or at which the events occurred (and for which the denominator population was at risk) must be included.

Infant mortality 'rate' for a given year should ideally include infants born alive who die in a given year in the same period born alive in the same calendar year. For rates, this would take care of the time element.

Activity 2.2.1 : Refer to relevant medical literature and get down the definitions of the following:

(1) Maternal Mortality Rate (MMR): Note that this relates to maternal deaths and childbearing.
(2) Infant Mortality Rate: (Note that this relates to children who die under one year of age) from any cause.
    a) Give reasons whether these are true rates or not.
    b) In MMR, the denominator is limited to live births, how does this affect the final value of MMR?

How to go about it:

(1) Examine the numerator and denominator and decide whether the numerator is part of the denominator or not.
(2) For example in MMR, does the denominator include all relevant exposure factors? E.g. it excludes pregnancy events that do not result in live births (different types of abortions, still births, ectopic pregnancies) yet maternal deaths resulting from these events would be included in the numerator. The denominator therefore excludes part of the population at risk and we end up with a smaller figure than actual figure. We tend to end up with an exaggerated bigger MMR than would otherwise be the case. MMR is a ratio not a rate.

References

(1) Foundations of Epidemiology by Lilienfeld
(2) Epidemiology by McMahon
(3) Principles of Epidemiology: a self-teaching guide by Roht LH, Selwyn BJ et al, 1982.

b. Rates, Ratios and Proportions commonly used to describe morbidity – Incidence and Prevalence

These two terms represent the most frequently used summary measures for the occurrence of morbidity in given populations. Incidence and prevalence are measures of morbidity i.e. pertain to sickness, disease or disability in specified populations. Events of sickness can be counted as a number of cases in a population to constitute a numerator. The denominator is concerned with the population at risk. However, the terms are also used for describing health related events that are not necessarily illness e.g. uptake of some desirable behaviours.

Activity 2.2.2

Based on your own prior knowledge of these terms how would you define incidence and prevalence. [Write your definitions down on a piece of paper]

Incidence

"The incidence of a disease is defined as the number of new cases of a disease that occur during a specified period of time in a population at risk for developing the disease during that period of time." [Refer to the book 'Epidemiology' by Leone Gordis for other definitions of Incidence]

Incidence per 1000 people in a population at risk =

$$\frac{\text{Number of new cases of a disease occurring in a population in a specified time}}{\text{Number of persons at risk of developing the disease during that period of time}} \times 1000$$

Here, the important word is **new cases**. Incidence is a measure of risk: The number of people at risk of developing the disease is the denominator and every member of this group has the potential of becoming a case and become part of the numerator. Because it includes only new cases, and occurring over a specific period of time, it is therefore a measure of the probability of acquiring the condition in the target population, over the period of review.

Now, some references refer to incidence as a rate. However, incidence is not a true rate. The denominator for incidence is usually the population at risk at the beginning of the follow-up period. It assumes that the entire population is followed up for the same period of time. However, during that period of time: Some people leave the population; others join the population or are born. Others who were not at risk at the beginning become at risk during the period. In addition, the time reference for incidence is a period of time, yet a rate is the occurrence of new cases 'per unit of time'. Therefore, when incidence is computed with a denominator that assumes uniform time of follow up, we often refer to this as 'incidence proportion' or 'cumulative incidence' or simply 'incidence'.

Incidence Rate: When used as a rate, TIME and PLACE must be stated and incidence is computed 'per unit time'. Because rates involve incidence per unit time, they are more specific. According to Roht et al, 'incidence' measures the development of a disease or health problem in a population (i.e. the frequency of new cases in the population at risk) during a specified period of time. Incidence rate on the other hand puts into consideration the total time over which each person has been exposed to the disease. This is expressed as ***person time of exposure.*** It could be hours, days, months or years. It therefore shows incidence 'per unit of time' and is called a rate because it shows how fast new cases are developing every moment of time. We say that time is expressed ***explicitly***. The formula is denoted as:

Incidence Rate (I) =

$$\frac{\text{No. Of people who get a diseases in a specified time period}}{\text{Sum of the length of time during which each person in Population is at risk i.e. the time each person is observed}} \times 10^n$$

(10^n = this is a multiple figure of 10 which could be 100, 1000, 100000 or any other figure)

Incidence rate must include dimensions of time (hours, days, weeks, months, years, etc.). The time at risk, is that time of observation of an individual that he/she is actually exposed, but remains disease free. The denominator is derived from the total sum of each individual's person-time for which he/she was free of disease and at risk during follow-up. If this time is in years, then we refer to the sum of person time as 'person years of observation'. If it is in weeks, we refer to person weeks of observation'. Incidence Rate is referred to in some references as 'Incidence Density'.

Incidence Density (Demonstration)

Dr Kato conducted a study that followed up 2000 men between the age of 30 and 45 years, 1000 of whom were smokers and 1000 were not, for a period of 5 years. By the end of the study period, 50 of the smokers and 22 of the non-smokers had developed erectile dysfunction. 400 of the smokers remained in the study for the entire period, 200 for 4 years, 200 for 3 years and 200 for 1 year. Half of the non-smokers remained in the study for 3 years and the other half for the entire period. Use this information to answer the questions that follow: (5Marks)

a. Calculate the incidence rate (per 1000 person years of observation), of erectile dysfunction in smokers
b. Calculate the incidence rate (per 1000 person years of observation), of erectile dysfunction in non-smokers:
c. Calculate the Relative Risk of developing erectile dysfunction in the two groups above

Working:

a. Calculate the incidence rate (per 1000 person years of observation), of erectile dysfunction in smokers:

Answer:

$$\frac{50}{400X5years+200X4years+200X3years+200X1year}X1000$$

$$=\frac{50}{3600}X1000$$

= 14 per 1000 person years of observation

b. Calculate the incidence rate (per 100,000 person years of observation), of erectile dysfunction in non-smokers:

Answer:

$$\frac{22}{500X5years+500X3years}X1000$$

$$=\frac{22}{4000}X1000$$

= 5.5 per 1000 person years of observation

c. Calculate the Relative Risk of developing erectile dysfunction in the two groups above:

Answer:

$$\frac{14}{5.5}$$

= 2.54

Attack Rate

It is defined as the cumulative incidence of infection during a defined time, such as the duration of the outbreak. Incidence rate is sometimes expressed as an attack rate usually presented as a percent. It is a special expression of incidence in populations observed for limited periods of time as in the case of epidemics. In such cases, the 'person time of observation' component is ignored, as it is known that the rate applies to the specific period of the outbreak and that everyone is at risk for the duration of the outbreak. We say that person time is expressed ***implicitly*.** In epidemics therefore, we often express incidence in form of an attack rate, without specific reference to time, since epidemics often occur over a relatively short span of time.

Prevalence

"Prevalence of a disease is the number of cases in a defined population at a specified point in time". Prevalence is defined as the number of affected persons present in a population at a specified time divided by the number of persons in the population at that time. Prevalence therefore includes both new and existing cases of the disease. It is a measure of the extent to which a disease persists in the population.

Prevalence per 1,000 people =

$$\frac{\text{No. Of cases of a disease present in the population at a specified time}}{\text{No. Of persons in the population at risk during that specified time}} \times 1000$$

Point prevalence and period prevalence: Prevalence is used in two ways either as "point prevalence or period prevalence". Point prevalence refers to the prevalence of a disease at a point in time while, period prevalence refers to people who had had the disease during a certain specified period of time which could be in weeks, months or years. Some of these people could have developed the disease before the period in question and entered that period with the disease before the period in question, while others developed it during the period in question. Therefore the numerator will include all those who developed the disease at some time and were captured during the period in question.

According to Roht et al (1982), "Prevalence measures the frequency of all current cases of disease in a population at a specified time". Current cases include previous cases and newly diagnosed cases. "Point prevalence, measures the frequency of all current cases of a disease at a given instant in time. Period prevalence measures the frequency of all current cases of diseases in a specified period of time".

***Point Prevalence*=**

$$\frac{\text{No. Of people with the disease at a specified time}}{\text{No. Of people in the population at risk at a specified time}} \times 10^n$$

***Period prevalence*=**

$$\frac{\text{No. Of people with the disease during a specified period of time}}{\text{No. Of people in the population at risk during a specified period}} \times 10^n$$

Relationship between incidence and prevalence

Note that prevalence will include both new cases of the disease at the time of say, a survey and old cases of the disease. This means that prevalence must be more numerical than incidence and

indeed incidence is a component of prevalence! The longer the duration of disease the more prevalent are the cases.

In a steady state in which the prevalence is low and does not vary much with time and in-migration is equal to out-migration:

Prevalence (P) ≅ incidence (I) x Average Disease duration (D) i.e. P ≅ I x D

This equation applies mainly in a steady state in which the prevalence is low and does not vary much with time. This equation does not apply in outbreak situations, or in diseases that show seasonality. This can be illustrated with Ebola disease, which kills its victims within 48 hours. Is its prevalence likely to be much bigger than its incidence? How close or far apart would the prevalence and incidence be? Now consider another case of a chronic disease like tuberculosis. Is prevalence likely to be much bigger or very near the value of the incidence? This is where the importance of disease duration comes in.

Practice Question:

In District X, there are 100,000 people. Previous studies have shown that TB incidence is 8 cases per 1,000 per year. If the average duration of TB is 21 months, the Prevalence of TB per 1000 population can be estimated to be:

a. 160 cases
b. 14 cases
c. 800 cases
d. Prevalence cannot be calculated because time of interest is not stated
e. None of the above

Application: Given any two of the components we can calculate the others. For instance, for some disease conditions where it is difficult to directly determine incidence, we can impute it from the other two parameters e.g. HIV new infections.

Problems with incidence and prevalence measurements: There are some problems associated with the use of these measurements, relating to the numerator and the denominator. These problems are either artefactual (errors in measurement) or real (changes in patterns of disease occurrence)

Problems with the numerator

a) ***Defining who has the disease:*** How do we define 'disease status' for a given individual or individuals in the population? There are often changing classification systems and case definitions. In 1994, the definition of AIDS changed drastically following a change in the case definition of AIDS that included a more sensitive tool – the CD4+ count.
b) ***Ascertaining who should be included:*** How do we find all the cases of the disease, new and existing? It may not be possible to trace all the cases as some diseases remain sub-clinical or if traced, the diagnosis may not be sensitive, there may be problems with recall or deliberate withholding of information, the interviewer may ask questions inappropriately, or if hospital data is used, it may exclude some potential cases.

Hospital Data:

- Hospital admissions are often selective

- Certain hospitals admit patients at a certain level of severity of the disease due to their referral level.
- The cases therefore may not be representative of the population
- Hospitals are not primarily planned for data collection; records may therefore not be applicable to research

Problems with the denominator

- ***Selective undercounting of population groups:*** Delinquents and mentally ill people may be left out in a census; Criteria in defining ethnic groups – is it by birth, language, origin, parents or residence – whichever we choose is likely to introduce an error.

- ***Cases in which some people in the denominator cannot be in the numerator:*** Should women who have undergone hysterectomies be included in uterine cancer studies?

Population at Risk

Activity 2.2.3
In our discussion above, especially with regard to denominators, we have talked of a population at risk from which cases of disease develop, later to become "new cases of disease" or incident cases and later to become a current case when we measure incidence and prevalence respectively. So, really, what do you understand by the term, "population at risk" in this sense? Put down your answer before you proceed.

We will now, consider the population at risk. Study the examples given in stage 1 and 2 below:

Stage 1:
Fig 1: This is the initial health population but with susceptible members
ᔑᔑᔑᔑᔑᔑᔑᔑᔑᔑᔑ = 11 people

Stage 2
Fig 2: Some of the susceptible individuals developed the disease
ᔑᔑᔑᔑᔑ = 6 people

In figure 2, five people are now sick who were susceptible and developed the disease of interest. The susceptible sub population could be the very young, the elderly or of certain sex or age or profession etc.

This may mean any of the following:

- A population or part of a population, which is susceptible to developing the disease of interest. This population can be defined on the basis of demographic factors such as women of reproductive age if one is interested for example, in contraceptive prevalence rate or any other family planning issues.
- Or can be on the basis of environmental factors like occupational exposures giving rise to certain occupational diseases. We use the term "population at risk" when we are usually describing rate of death or disease in a given community composed of susceptible people to a disease at a specific period of time. When we talk of a population at risk, we are also thinking of people known or thought to be susceptible to a disease or a health problem in a given period of time. We can therefore talk of total or subgroups of populations. In cases like these, the population at risk could be persons who are present, susceptible to but are free from the disease at the start of a given period. Is it surprising to you, that a population

at risk is usually a denominator? When measuring disease in a community (or death i.e. mortality), by convention, the population at risk is the average population of the community exposed for a given period of time. The average population represents an estimate of the population of that community though to be alive on July 1st of a calendar year.

- If we consider more than one year of observation, we find the average of mid-year estimates of the observed period to be the population at risk over that period. Why do you think we do this? Why do you also think the 1st of July population is important? Well, we want to take into account the dead, the newborns, the in-migrants and the out-migrants between 1st January and 31st December of a calendar year.

EXCERCISES

EXERCISE 2.2.1 Defining Population at Risk

Now that you know what a population at risk is, and based on your knowledge of the natural history of disease, suggest a population at risk for the following (if you wanted to investigate these in the community):

b) Deaths due to lung cancer
c) Births

EXERCISE 2.2.2 Calculating the Population at Risk

A community is composed of 100,000 persons, 20% of whom are women aged 35 years and above, 10% are females aged below 35 years, 15% are males aged 45 years and above and 5% are both males and females who are heavy smokers, and 8% are prostitutes. From your knowledge of diseases listed below, state the "population at risk" for each group of diseases and state your assumptions. (You may read about these diseases to update yourself).

a. Breast cancer
b. Bronchial carcinoma
c. HIV/AIDS

EXERCISE 2.2.3 Application of the concept of population at risk in interventions

You have been given a consultancy by Uganda Family Planning Association to evaluate the impact of their family planning programme specifically targeting the age group up to 19 years of age. Its programme specific objective was to ensure that no girl child in Uganda should get pregnant before the age of 19 years. You have now decided that you will use the birth rate and possibly pregnancy rate as one of your indicators of success or failure of the programme.

a. What would be a rate of total success?
b. What age group(s) would you consider to be the population at risk and therefore appropriate for your study population? Give reasons for your answer.
c. Given the programme objectives and potential exposure risks, list factors likely to influence the level of your indicator(s) (i.e. birth rate or pregnancy rate).
d. If you were calculating birth rate or pregnancy rate, who would you consider forming your denominators and whom would you exclude?

EXERCISE 2.2.4 Incidence and Prevalence

You should now look at ways of calculating incidence and prevalence rates now that you are familiar with these concepts. Try to reflect how you would use these rates for planning or for any other actions/decisions, if you were the District Director of Health Services. Think

about a few scenarios. Now study the following situation and use your background knowledge to solve the problems that follow:

A first-year class of MPH students was 200. During the month of January, 2002 some students developed malaria fever. Calculate the relevant rates of disease in this class from the following information:

On 31st December 2002, 10 students reported to class with malaria fever but continued to attend class while on treatment and fully recovered by 5 January 2003. By 15 January 2003, twenty other students had also developed malaria and five of these had to miss class. During the entire period of January 2003, i.e. from Ist to 31st, forty different students had developed malaria and ten of these had missed classes.

(1) Calculate point prevalence of malaria on 1st January 2003.
(2) Calculate point prevalence of malaria on 15th January 2003.
(3) Calculate the period prevalence rate of malaria 1st up to 15th January 2003.
(4) Calculate the incidence of Malaria in January 2005
(5) Calculate the cumulative incidence rate of malaria in January 2003.
(6) If 10 students started malaria prophylaxis on 10th January, and another 10 students started prophylaxis on 20th January, calculate the incidence rate of malaria for January (Assume that once prophylaxis is initiated, a student is no longer susceptible)

Answers to Activities

Answers to Exercise 2.2.1

a) Death due to bronchial cancer: That community's media population people known to be smokers would be the population at risk.

b) Birth: population at risk will be number of women of childbearing age or number of women who are of childbearing age and who are sexually active and not using contraceptives.

Answers to Exercise 2.2.2

a) Breast cancer: Persons at risk of breast cancer are women aged $\geq$ 35 years
$= \frac{20}{100} \times 100{,}000 = 20{,}000$

b) Prostatic carcinoma: Population at risk = 15% men who are $\geq$ 45 years which
$= \frac{15}{100} \times 100{,}000 = 15{,}000$

b) HIV/AIDS: Population at risk are prostitutes (others who could be at risk are their spouses and their unborn babies) $= \frac{8}{100} \times 100{,}000 = 8{,}000$

Answers to Exercise 2.2.3

a) Complete success would yield 0% birth rate or pregnancy. The Family Planning Programme would have achieved its target.

b) Population at risk and therefore suitable for study, should have started going in their menstrual period who would be thought to be at risk of pregnancy if they got into sex activities. Age 14 years could be assumed to be average age for menarche although some girls get there earlier. Therefore, age 14 to 19 would be considered the risky age

on assumption that they practiced sexual intercourse. Susceptibility and exposure would there use menarche and sexual activity.

c) Factors to influence birth rates or pregnancy rates would be: knowledge and use of Family Planning methods e.g. pills, condoms, abstinence, frequency of sexual contacts, % no. Of abortions, availability and accessibility of Family Planning services, sex education, etc.

d) The denominator would be the population at risk. This could be girls aged 14 – 19 who we know potentially can get pregnancy if exposed to the risk i.e. unsafe sexual activity. Therefore mid-year population of this age group should constitute the denominator. Males in this age group do not qualify because they are not susceptible to getting pregnant.

Answers to Exercise 2.2.4 (N.B. – Many alternatives are possible)

Incidence implies people who were free from disease at the beginning have now developed it during a given period; it gives an estimate of risk of developing the disease. Prevalence, on the other hand describes the amount of disease (the disease burden) in a population at a point in time or in given period of time.

If the incidence rates increase, clues as to the causal or risk factors might be possible if exposures prior to the disease are discernable. This may help in instituting control and preventive measures. On the other hand, an observed trend of decreasing incidence rate might reflect the success of the effect of control measures, while increase might reflect failure in the control programmes or changes that have emerged in the agent/lost dynamics and therefore calling for re-examination of the control programme.

The rising incident rates may also imply the reporting procedures for cases have improved, or better diagnostic methods with better sensitivity might now be in place, improving case-identification or case-finding. All these call for the attention of the District Director of Health Services' (DDHS) actions/interventions. Prevalence data, on the other hand, will help the DDHS estimate the magnitude of disease problem and may identify high-risk groups and areas most affected in his/her district. This will form the basis of prioritising his/her interventions.

Calculations:

a) Point prevalence on 1st January 2003 = $\frac{\text{no. of malaria cases}}{\text{Population at risk}} \times 10^n = \frac{10}{200} \times 100$

= 5%.

(Malarial cases spilled over from December 31st)

b) Point prevalence on January 15th = $\frac{20}{200} \times 100$

(The other 10 had recovered and therefore not part of the numerator) = 10%.

c) Period prevalence up to the 15th January = $\frac{10 + 20}{200} \times 100$

(10 from 31st December who spilled over from January + 20 of them)

$= \frac{30}{200} \times 100 = 15\%$

d) Cumulative Incidence rate of malaria is = $\frac{40}{200 - 10}$ (10 were ill in December 2003) = 190

$$= \frac{40}{190} \times 100 = \frac{400}{} = 21\%$$

e) Incidence Rate for Malaria in January is = [Pease use your knowledge to calculate]

References

1. Basic Epidemiology by R. Beaglehole et al
2. Epidemiology: Leon Gordis
3. Foundations of Epidemiology by Abraham Lilenfield
4. Epidemiology in Medicine by Charles Heinekens

c. Common Rates, Ratios and Proportions used to describe Mortality

We shall now look briefly at some mortality measurements

Mortality measures: Common measures of mortality include the following:

(a) Annual Mortality Rate from all causes =

$$\frac{\text{Total deaths from all causes in 1 year}}{\text{No. Of persons in population at mid-year}} \times 1000$$

Significance of annual mortality rate: This is a measure that reflects the total death rates from all causes in a population in a year. However, it does not show the changes in age structure of the population over time.

(b) Case Fatality rate

$$\frac{\text{No. Of Individuals dying during a specified period of time after disease onset or diagnosis}}{\text{No. Of individuals with specified disease}} \times 100$$

Significance of the case-fatality rate: The case-fatality rate is an important parameter as it gives important insights into disease control especially in epidemics: A high case fatality may be due to a very virulent strain of the disease agent. However, it may also indicate serious gaps in case management including supportive treatment.

(c) Proportionate Mortality (This, as you can see is a ratio)

$$\frac{\text{Number of deaths from a particular cause in a year}}{\text{Total deaths in a year}} \times 100$$

Significance of proportionate mortality: Proportionate mortality tells us about the cause that accounts for most deaths and their contribution to overall mortality.

Problems with mortality data: Like morbidity data, mortality data has some problems. We can highlight a few of them as follows:

- Problems with non-uniformity of reporting for instance different ways of reporting on death certificates. Different clinicians may have different ways or reporting the causes of mortality.
- Revision of classification systems
- Non-consistent recording and unreported deaths

d. Other rates/Specific Rates

There are many other types of rates that measure events. These include Natality rates (e.g. birth rates and pregnancy rates). If we put a restriction to a particular rate, it is then called a specific rate, e.g.:

> **Annual Mortality Rate from Leukaemia in children younger than 10 yrs (per 1000 population) =**
>
> $$\frac{\text{No. Of deaths from leukaemia in one year in children under 10 years}}{\text{No. Of children in the population younger than 10 years at mid year}} \times 1000$$

This is an age/cause specific rate. You can see that more than one restriction can be put. [These concepts will further be expounded on in the module on Demography and Population Dynamics]

e. Sources of data for computation of rates, ratios and proportions

In order to compute rates, ratios and proportions we need data on the health-related event occurring in the population. Where do we obtain this data? Epidemiological data is obtained in three main ways: 1) We can obtain data from population-based surveys conducted at a point in time or multiple time points. We shall discuss this further when we look at epidemiological study designs. 2) We can obtain data from surveillance, either by setting them up or using existing surveillance systems. We shall explore this further when we discuss principles of surveillance. 3) We can obtain data from registration systems e.g. vital statistics registers. This is discussed further in the course on Demography and Population Dynamics.

Lesson 2: Standardisation of Rates

Introduction: When comparing two or more populations, or one population at different time periods, it may be important to standardise the rates used in comparison. This is because the two populations may have un-equal composition with regard to another factor that is not of interest, yet that factor could influence the outcome we are comparing. For instance, we may want to compare mortality levels in two countries at different levels of development. However, the more developed country could also have a much older population, yet age is also associated with death. This section describes techniques that can facilitate the comparison of populations that are non-homogenous.

Lesson Topics:

a. Types of rates
b. Importance of standardisation of rates
c. Direct Standardisation
d. Indirect Standardisation

Lesson Objective(s)

The MPH student should be able to:

- Distinguish the different types of rates
- Illustrate the importance of standardisation of rates
- Apply standardisation techniques to compare data from two or more non-homogenous groups

a. Types of rates

In the previous section, we saw the meaning of rates, ratios and proportions and how they are used to summarise the health related status of a community. In general, there are two main types of rates:

a. Crude rates
b. Specific rates

Crude rates are obtained by relating the number of events by the whole population.

Example: Number of births per 1,000 persons in the Ugandan population is a crude birth rate.

Activity 2.2.4

Give two more examples of a crude rate

Specific rates are obtained by relating the number of events by each sub-group of the population between which rates are likely to differ.

Why do we need to standardize rates? When we compare crude rates/ratios between populations, we might get erroneous results because the rates we are comparing might be affected by another factor (e.g. age, sex, education level etc.) that is not of current interest to us yet that factor could be distributed differently between the two populations. That silent factor might be the one causing the differences in the crude rates between the two populations. To compare the rates between the two populations, we need to 'standardize' their composition, so that differences in composition are resolved i.e. so that we compare 'apples with apples' not 'apples and oranges'.

What does standardization mean? Standardization is a general term used in the analysis of rates to mean procedures for controlling for the effect of differences in population composition due to age, sex, etc. By standardisation, we adjust for other differences in data to be compared, so that the rates we obtain are not affected by the differences in profile between the groups to be compared.

Methods of standardizing rates: There are generally two methods of standardizing rates: Direct Standardization or Indirect Standardization

c. Direct Standardization

DEMONSTRATION A

Look at the mortality data in the table below. The data shows mortality statistics for two countries: A 'high income country A' and a 'low-income country B'. The table shows both the total deaths for each country as well as the age-specific deaths. It also shows the sizes of the target population (the denominator) both the total and the stratum specific sizes. These are used to compute the age specific death rates as well as the overall crude death rates for each country. These are presented in the table below:

	High income country A				**Low income country B**			
Age in yrs	Deaths in pop	Number	% of pop	Death rate/1000	Deaths in pop	Number	% of pop	Death rate/1000
<15 yr	1028	538480	30.4	1.9	236	103004	34.3	2.3
15-44 yr	1629	728363	41.1	2.2	388	149964	49.9	2.6
45-64 yr	3839	341956	19.3	11.2	436	40699	13.5	11
≥65 yr	8358	162094	9.1	51.6	368	6715	2.2	54.8
Total	**14,854**	**1,770,893**	**100%**	**8.4**	**1,428**	**300,382**	**100%**	**4.8**

Guiding question 1: Examine the data; how do you interpret it. What is your initial impression of the Crude Death Rates as compared between the two populations. How do the two populations compare when we consider the age group specific mortalities?

Feedback: You can see that the death rates in all age categories are higher in country B than in country A; however, the overall mortality (crude death rates) is higher in country A than in B. There is thus a problem in the interpretation of these findings if we are to rely on the Crude rates

Guiding question 2: Why does a difference in the age structure of these two countries A& B make it preferable to standardize the rates before making further comparisons?

Feedback: In calculating the crude death rates for the two populations, we do not cater for the fact that age in itself affects mortality. There is increasing likelihood of death as one gets older. Thus, the crude death rates do not take into account the fact that the two populations are stratified differently. Population A has a higher proportion of older people 65 years and above (9%) than population B (2%) and we have highlighted that old age is in itself a risk factor for dying. It is therefore necessary to keep the sizes of the different age groups a constant as we compare the mortality in the two populations

Guiding question 3: In general what condition must prevail so that it is necessary to adjust or standardize for age or other factors?

Feedback: When there is a characteristic that differs in the populations that are being compared and this characteristic in itself an effect on the rate we are determining, then it is necessary to standardize and hold that factor constant.

Using direct standardization to adjust for the differences in population structure: To do ***direct standardization,*** we get the strata specific rates, e.g. mortality rates for each age group, and apply them independently for each of the comparison population to a similar hypothetical standard population, to gauge what would be the actual number of events had the sizes of the strata in the two comparison populations been the same. We therefore calculate the expected deaths where they to have a structure like the standard population in each stratum and then total them up, to enable us determine the ***Adjusted Rates*** for the population of interest. We then use the adjusted rates to compare.

Using the following standard population and appropriate data in number one above, we are going to use the direct method of standardization to adjust for the differences in age structure of the comparison populations:

		A		B	
Age in yrs	Standard population C	Age specific Death rate/1000	Expected Deaths	Age specific death rate/1000	Expected deaths
< 15 yr 15-44yr 45-64 yr ≥65	58,017,845 83,270,951 41,820,193 20,101,169	1.9 2.2 11.2 51.6		2.3 2.6 11 54.8	
Total	203,210,158				

Guiding question 4: Complete the table above by applying the age specific death rates computed in the previous table for both Country A and Country B to the sub-population sizes in a similar standard population C to adjust for the different age stratification in the two populations.

Feedback: The table is thus completed as follows:

		A		B	
Age in yrs	Standard population C	Age specific Death rate/1000	Expected Deaths	Age specific death rate/1000	Expected deaths
< 15 yr 15-44yr 45-64 yr ≥65	58,017,845 83,270,951 41,820,193 20,101,169	1.9 2.2 11.2 51.6	110,234 183,196 468,386 1,037,220	2.3 2.6 11 54.8	133,441 216,504 460,022 1,101,544
Total	203,210,158		1,799,036		1,911,511

Guiding question 5: Calculate the age-adjusted death rate per 1000 in country A and B.

Feed-back:

Adjusted death rate country A (per 1000) = $\frac{\text{Total Expected Deaths in A}}{\text{Total standard popln}} \times 1000$

$\frac{1,799,036}{203,210,158} \times 1000 = 8.85/1000$

Adjusted death rate country B (per 1000) = Total Expected Deaths in B x 1000
Total Standard popln

1,911,511 x 1000 = 9.41/1000
203,210,158

Guiding question 6: What information does the age-adjusted rate convey?

Feedback: While the crude death rates showed that mortality was higher in population A than in B, the adjusted rates actually show that mortality is higher in population B than in A.

Remember!
To do ***direct standardisation,*** we get the strata specific rates (e.g. mortality rates for each age group) and apply them independently for each of the comparison population to the same hypothetical standard population, to gauge what would be the actual number of events, had the strata in the two comparison populations been the same. We therefore calculate the expected deaths in each age group and then total them up, to enable us determine the ***Adjusted Rates*** for the population of interest, were it to have a similar structure to the standard population; we then use the adjusted rates to compare.

d. Indirect Standardization

In the previous section, we saw that to conduct Direct Standardization, we need to have the age-specific rates for both populations that we want to compare – it is both of these that we apply on the standard population. However, very often, one of the countries we are trying to compare lacks data on age specific rates, though the total deaths might be known. This is often common for low income countries where registration systems are patchy and incomplete for some variables. You may therefore get a situation where one country has all the stratum specific deaths while the comparison country does not have. What would we do to standardize the rates in this case? We use 'Indirect Standardization'.

DEMONSTRATION B

The following data shows the population distributions and mortality by age for a South American Country and USA at the point in time. Numbers of deaths for each age group in the S. American country were not registered. Use indirect method of adjustment to answer the questions that follow.

	S. America			**USA**			
Age in yrs	**Population**	**% of total**	**Deaths**	**Population**	**% of total**	**Deaths**	**Age specific death rate/1000**
< 5 yr	3,789,000	17.5	*	17,115,336	8.4	86,215	5.0
5–14	5,932,000	27.5	*	40,902,509	20.2	16,847	0.4
15-44	9,714,000	44.9	*	83,270,951	40.9	157,071	1.9
45+	2,169,000	10.1	*	61,921,362	30.5	1,660,179	26.8
	21,595,000	**100**	**165,812**	**203,210,158**	**100**	**1,920,312**	**9.4**

* Data not available

Guiding Question 7: Calculate the Crude death rates for each of the two countries. Do you think age adjustment is necessary, if yes or no why?

Feedback:

Crude death rate (per 1000) = Total deaths x 1000
Total population

S/America: CDR = 165,812 x 1000 = **7.67/1000**
21,595,000

USA: CDR = 1,920,312 x 1000 = **9.45/1000**
203,210,158

Yes, age adjustment is necessary because in comparing the two populations another factor that affects mortality comes into play and this is the age of the population. We see that USA generally has an older population above 45 yrs (30.5%) than South America (10.1%). We also know that old age is in itself a risk factor for dying. It is therefore necessary to standardize for age stratification so that this is held constant as we compare the two populations

Guiding Question 8: Generate another table for the South American country for each of the age groups. Apply the age specific American rates to calculate the expected deaths in each age category for the South American Country i.e., if you assumed that the South American country's population was dying at the same rate as Americans in each age category, how many deaths would occur in each age-group and in total?

Feedback: Calculation of the age specific American death rates/1000 is as follows:

Deaths in age group X 1000
Population in age group

Calculation of expected death rates for age groups in South American country using American Rates:

Expect. Deaths for age group = Age spec. Amer. Death Rate X Pop. in age group
1000

The table is thus filled as follows:

Age in yrs	Population S. American Country	% Of total	Deaths	Age specific American Death rate/1000	Expected Deaths for South American country using American rates
< 5 yr	3,789,000	17.5	*	5.0	18,945
5–14 yr	5,932,000	27.5	*	0.4	2373
15-44 yr	9,714,000	44.9	*	1.9	18,457
45+	2,169,000	10.1	*	26.8	58,129
TOTALS	**21,595,000**	**100**	**165,812**		**97,904**

Guiding question 9: Calculate the age adjusted rate /1000 for the S. American country.

Feedback:

Age adjusted rate for the S. American country/1000 =
97,904 X 1000 = 4.5/1000
21,595,000

This implies that if this population were dying at the same age specific rates as the USA, their overall mortality (4.5/1000) would be much less than that of the USA (9.4/1000)

Guiding Question 10: Use the SMR to compare mortality as follows:

a) Calculate the Standardized Mortality ratio (SMR) for the S. American country. Comment on it.

Feedback:

$$SMR = \frac{\text{Observed Deaths}}{\text{Expected Deaths}} \times 100$$

$$= \frac{165{,}812}{97{,}904} \times 100$$

$$= 169$$

This SMR is greater that 100.

b) What does an SMR greater than 100 mean?

Feedback: An SMR greater than 100 means the observed number of deaths exceeds the expected number of deaths. It also implies that the mortality in that population is greater than the mortality in the population used as a standard.

c) What does an SMR less than 100 mean?

Feedback: An SMR less than 100 means the observed number of deaths is less than the expected number of deaths. It also implies that the mortality in that population is less than the mortality in the population used as a standard.

Guiding question 11: In what circumstances would it be necessary to use the indirect rather than the direct method to adjust rates?

Feedback: The indirect method would be used when information on strata specific characteristics in the population that is being studied, like in this case the age specific mortalities, is not available or is incomplete.

Remember!
To do ***indirect Standardisation,*** we first examine the ***Observed rate*** e.g. Observed Mortality in the population of interest. We then apply the stratum specific rates of a standard population to our population of interest, and calculate the ***Expected rate*** if the study population were similar in structure to the standard population. We then calculate the ***Standardised Ratio***, which we use for comparison e.g. Standardised Mortality Ratio:

$$SMR = \frac{\text{Observed Deaths}}{\text{Expected Deaths}} \times 100$$

An SMR > 100 suggests more mortality than the expected
An SMR < 100 suggests less mortality than the standard population

SMRs are particularly useful in investigating Occupational Health Events

Advantages and disadvantages of standardization

Direct Standardization	Indirect Standardization
Computationally easier	Computationally not as easy as in direct standardization
Requires a third population that might be	Does not require a third population that might be

difficult to get. However this requirement might be overcome by "adding" the two populations to perform standardization	difficult to get
Using a third population as a standardizing population makes it independent of any compositional abnormality in the two populations whose rates are being compared	Both populations being compared might have unusually abnormal compositional structure, thus making generalizability difficult
Requires the knowledge of stratum specific rates, which are then applied to a standard population in both populations being compared.	Requires only knowledge of the stratum specific rates in the standard population
NB: The adjusted rates we obtain after standardisation are only relevant for that particular comparison, and may not be useful for reporting purposes or for other comparisons	

Exercise 2.2.1: Direct and Indirect Standardization of rates

Please go through the Exercise 2.2.1. It is contained in your **additional resources folder**. It shows a step-by-step process on the approach to direct and indirect standardization. By the end of this exercise, you will have appreciated fully what we mean by standardization of rates. It is advisable that you attempt each question and discuss with your colleagues

Summary

1. We have defined a rate, and explained how different it is from a ratio
2. We have demonstrated the difficulty of fairly comparing rates when the compositional structure of the populations whose rates are being compared is different. Thus, the need for standardizing the rates
3. There is a need standardize the rates if the compositional structure of the populations differs by a factor related to the rate
4. We have seen the two different methods of standardizing:
   a) Direct standardization
   b) Indirect standardization

REFERENCES

1. Barker DJP, Hall AJ (1991) Practical Epidemiology. (Educational Low-Priced Books Scheme – 4th Edition)

Session 3: Validity and Reliability of Screening Tests

Introduction: In public health and disease control, identification and early treatment of people with some disease conditions is essential for prevention of disease spread. This is achieved through screening. For screening programs to be viable and effective, we need not only to have affordable tests that can be applied to large sections of the population but these tests need to be accurate in identifying people with disease and those without. The challenge is therefore, how to we evaluate the accuracy of screening tests before they are rolled out for primary care use. In this session, we shall discuss the processes involved in assessing validity and reliability of screening tests.

Lesson Topics

a. Background: Why validate measurements?
b. Validity of Measurements: Sensitivity and Specificity of Tests
c. Validity of Measurements: Predictive value of Tests
d. Reliability of measurements

Lesson Objectives

By the end of this lesson, the MPH student should be able to:

1. Explain the importance of validating the tools used in epidemiological measurements
2. Employ sensitivity and specificity in validating epidemiological measurements
3. Interpret the calculations of predictive value of epidemiological tests and their relationship to disease prevalence and specificity
4. Compare tests of different sensitivity and specificity so as to select appropriate tests for the different forms of screening programmes
5. Illustrate the importance of reliability in epidemiological measurements

a. Background: Why validate tests?

The health sciences utilize the technique of measurement extensively. The nature of the measurement varies across the different disciplines and it includes clinical assessments (history and physical examination), physical measurements (say weight, height, length) and laboratory assessment. It also includes the frequency of diseases or physiological conditions in populations, laboratory measurements and many other types of measurement. All in all, every procedure we conduct, for the purpose of coming to a diagnosis, is a test. However, the procedures differ in their level of accuracy and certainly certainty.

Clinical assessments and laboratory tests: Clinical assessment may provide a provisional diagnosis, which may be confirmed by other types of measurements. This means that clinical assessment may be less valid than other types of measurement such as laboratory tests.

Fig 1.2 Are you OK?

The validity of a clinical assessment should be a concern for every clinician.

Laboratory Samples: While laboratory tests are being used more extensively for diagnostic purposes, the validity of those tests should be a concern of every one using them. One important public health application of laboratory tests is in screening programmes for diseases of public health importance.

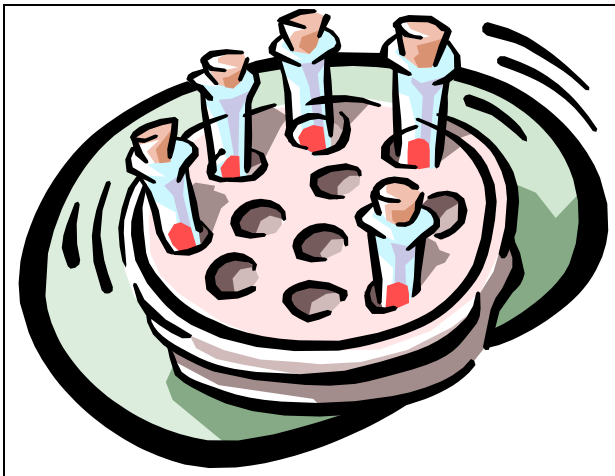
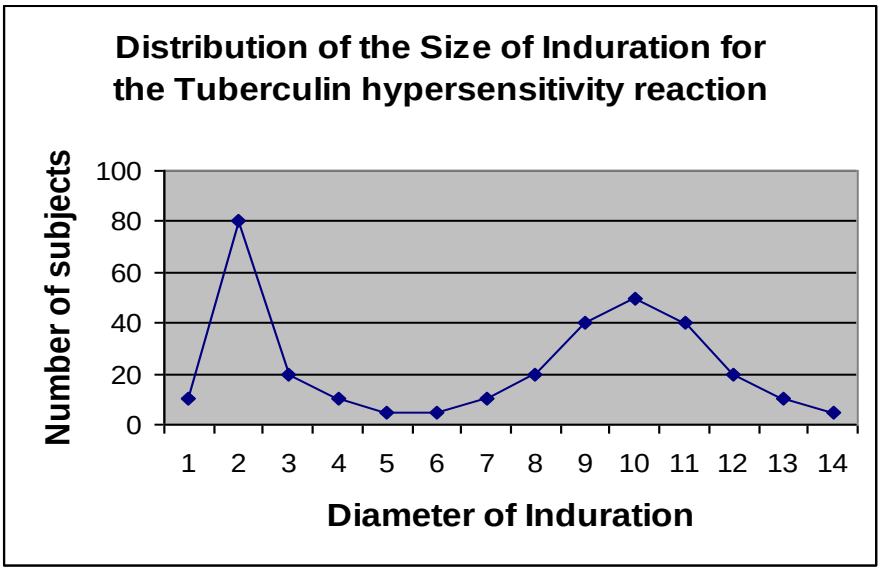


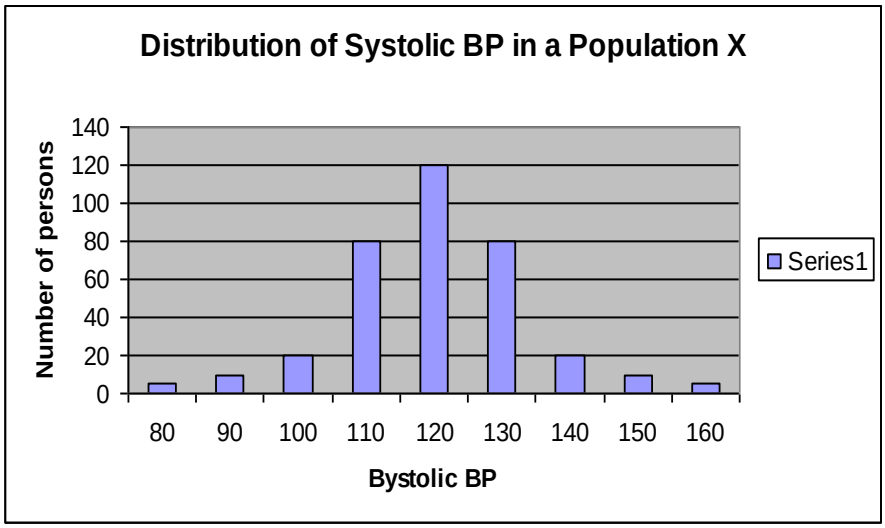
Fig 1.3 The Lab samples

Biological variations in populations: Individuals differ biologically and as such, continuous variables are often distributed as ranges [Refer to the Normal Distribution in the next module: Applied Biostatistics]. The normal distribution is ***unimodal;*** there are however some ***bimodal*** distributions, e.g. the distribution of the diameter of in durations in the tuberculin reaction.

Example of Tuberculin Reaction: Bimodal Distribution



Example of Systolic BP: Unimodal Distribution



Because of these variations, we can use these curves to establish "cut-offs" and ranges in which we are certain that the majority of people lie. However, by establishing ranges, we tend to exclude those people who are otherwise normal, but lie in the extremes (outliers). If we then apply these cut-offs in deciding normalcy, there is a probability that some "normal" people will be incorrectly classified as "abnormal" because they are at the extremes. A robust test minimises this error while a non-robust one will exaggerate it: This is the basis for validity.

Why validate screening tests? Population level screening is a very important part of public health practice. However, there are a number of challenges with screening to identify people with disease, one of which is the question of 'which test to use'. In order to screen as many of the population as possible, we need cheap, acceptable, less invasive but highly accurate tests. Applying expensive tests for massive screening would be a non-starter as it would result in prohibitive costs of the health system. On the other hand, cheap tests are almost always lacking in accuracy. Because less costly tests are inevitable, epidemiologists would like to develop new and cheaper versions of these tests so as to identify as many diseased persons as possible – but before rolling them out for public

health use, they need to be validated. This session discusses the science behind testing the validity of screening tests before they are put out for large scale use.

A word of caution: Whenever you make a measurement you should think about how closely that measure reflects the actual truth. Think about any measurement that you may have made or that you asked for. This could be temperature, weight, glucose concentration etc. Was the result you got the real truth? Could it change if the measurement was repeated several times? It is common to record some variation when a measurement is repeated several times. Validity of measurements should always be a concern in the following types of measurement or assessments.

b. Validity of Measurements: Sensitivity and Specificity of Tests

Validity: The validity of a measurement or test is the extent to which it measures correctly what it is intended to measure OR, the ability of a test to correctly differentiate between who has a particular health related condition and who does not. It has two components:

1. Sensitivity: The ability of a measurement to identify correctly those who **actually have** a particular condition

2. Specificity: The ability of a measurement to identify correctly those **who do not have** a condition.

How do we measure validity of a test?

To validate a measurement, we use another test considered the "Gold Standard" in proving the condition, but which cannot be used routinely because of its invasiveness or expensiveness. We conduct a validity study by comparing the performance of the test too a Gold standard. We obtain an adequate sample of the population and subject it to the 'Gold Standard'. The Gold Standard determines: Those who in reality have the condition (e.g. disease) of interest and those who do not have. We then apply the test that we are validating – to both those who have been determined by the Gold Standard to have the condition, and those who have been determined not to have the condition.

The 2X2 table for validity: If we use a dichotomous scale, we can represent the findings in a 2X2 epidemiological table as follows:

		Disease Status		
Test Result		**With Disease**	**Without Disease**	
	+ve	a (TP)	b (FP)	(a+b) or (TP + FP)
	-ve	c (FN)	d (TN)	(c+d) or (FN + TN)
		(a+c) or (TP+ FN)	(b+d) or (FP + TN)	(a+b+c+d)

TP= True Positives; **FP**= False Positives; **FN**= False Negatives; **TN**= True Negatives

$$\textbf{Sensitivity} = \frac{TP}{TP + FN} \quad \text{or} \quad \frac{a}{(a+c)}$$

$$\textbf{Specificity} = \frac{TN}{FP + TN} \quad \text{or} \quad \frac{d}{(b+d)}$$

Therefore, using probability theory:

Sensitivity: Probability of testing positive when one has the disease (or proportion of persons who are actually ill, that the test correctly detects)

Specificity: Probability of testing negative when one has no disease (or proportion of persons who are not actually ill that the test correctly identifies as negative)

This form of 2X2 table will be used in many other analyses.

Example 2.2.2:
Imagine a population of 500 people of whom 100 actually have a disease and 400 do not have the disease. Imagine also that all the 500 people are subjected to a screening test that is capable of identifying positive cases, with the following results.

Table 1.8

	True Characteristics in the population		
Results of screening	**Disease**	**No Disease**	**Total**
Positive	90	110	200
Negative	10	290	300
Total	**100**	**400**	**500**

Note that although only 100 people have the disease, the result of the screening test was that there are 200 people with the disease. The test categorized many people who do not have the disease as diseased. From this table therefore:

Sensitivity = 90/100 * 100 = 90%

Specificity = 290/400 * 100 = 72.5%

EXERCISE 2.2.5: Calculation of sensitivity and specificity
Assume a population of 1,000 people, of whom 100 have a disease and 900 do not have the disease. A test is available that can yield either positive or negative results. We want to use this test to try to separate persons who have the disease from those who do not. The results obtained by applying the test to this population of 1,000 people are as shown in the table below:

Table 1.9

	True Characteristics in the population		
Results of screening	**Disease**	**No Disease**	**Total**
Positive	80	100	180
Negative	20	800	820
Total	100	900	1,000

2) What is the sensitivity of the screening test?
3) What is the specificity of the screening test?
4) What is the positive predictive value of the test?

Dealing with continuous variables: So far, we have been dealing with discrete dichotomous variables. When dealing with continuous variables (e.g. Blood sugar or Blood pressure), the challenge is even greater. The decision is made basing on cut-offs.

- A high cut off will be more specific i.e., will identify more of those without the condition. It will however not detect some people with the condition, hence reduced sensitivity e.g., a

high cut off for blood sugar will detect all with a normal blood sugar, but classify a good number of those with low glucose tolerance as normal

- A low cut off will be more sensitive i.e., will identify more of those with the condition, but will include many who do not have the condition (reduced specificity) e.g., a low cut off for systolic BP will include all with a high BP but also a good number with normal BP.
- In choosing a cut off therefore, the epidemiological mind should strike a balance based on the potential effects of declaring false results

Consequences of False Test Results

If we roll out a test for mass use in public health screening, we are liable to many challenges, especially those arising from false positives and false negatives.

False Tests: Do unto others what you would like to be done on you	
<u>False Positivity</u> -Emotional/Psychological -Burdening the health system -It is difficult to undo one's thinking is the true situation is discovered	<u>False Negativity</u> -A potentially serious condition may be missed
-Think about telling someone that they are HIV positive when they are not	-Think about missing early cancer of the breast or cervix, which would be cured if detected at the earliest histological staging

It is therefore important that for conditions where the opportunity cost and ethical implications of false results is high, we ought to validate the primary care screening test before rolling it out for mass use. This helps us to know the level of accuracy with which the results of the tests should be interpreted.

Improving validity – Multiple testing/measurements: We can improve the validity of epidemiological tests by conducting multiple tests. These tests may either be sequential or simultaneous

a) Sequential (two Stage) measurements

In sequential testing, a less expensive, less invasive test is performed first, and then all those who test positive are subjected to a second more invasive test. In such cases, we have an overall gain in net specificity, but a loss in net sensitivity as illustrated below:

Example 2.2.3: ***Calculation of net sensitivity and net specificity***

Consider the following scenario:

Test 1: if: **Sensitivity** of this test is 70%
Specificity of this test is 80%
Total Population: 10,000
Prevalence of diabetes in population (Known): 5% therefore those with diabetes are 500

When we apply this test, with the above sensitivity and specificity, we are likely to get the following (Please do the calculations yourself so as to know how the figures in the table are arrived at:

	True Characteristics in the population		
Results of screening	**Disease**	**No Disease**	**Total**
Positive	350	1900	2250
Negative	150	7600	7750
Total	500	9500	10,000

We then subject all the positives (2250) to a second test

Test 2: if: **Sensitivity** of this test is 90%
Specificity of the test is 90%
Total Population: Positives retested = 2250
Prevalence: In the first test, those with actual diabetes were 500; in the second test however, we exclude those who tested negative. Therefore, those with actual diabetes are 350, meaning that the rest do not have (1900). We then fill in the newly computed figures. (Please confirm the calculations to get a feel of what we are doing)

	True Characteristics in the population		
Results of screening	**Disease**	**No Disease**	**Total**
Positive	315	190	505
Negative	35	1710	1745
Total	350	1900	2250

Therefore: **Net sensitivity** = 315/500 X 100 = 63%
Overall ***reduction*** in net sensitivity

Net specificity = 7600(from test 1) + 1710 (from test 2)/ 9500 X 100 = 98%
Overall ***increase*** in net specificity

b) Simultaneous (series) measurements

In simultaneous testing, the same sample is subjected to different tests. For one to be negative, they have to pass all the tests as negative (overall loss in specificity). One is positive if they fail any of the several tests (overall gain in sensitivity)

c. Validity of Measurements: Predictive value of Tests

In Public Health we are interested in screening populations to find what proportion is affected by a disease, so as to inform the intervention process e.g. we want to correctly identify as many people with the latent typhoid or cholera or TB infection (careers) so that they are treated and do not spread the condition. We are therefore more interested in sensitivity and specificity.
Very often however in public health and clinical practice, it quite common to start with less robust tests and then work upwards towards the gold standard if the initial test does not give us sufficient confidence or if there is no improvement with treatment. In such cases therefore, we are interested in answering the question: if the clinical test is positive, is this patient actually ill?

Examples:
When a patient comes to the clinic complaining of fever with rigors and chills, many rural clinics make a diagnosis of malaria. In this case, the clinical assessment is a form of screening test. However, we may go further to conduct a blood slide/microscopy to confirm if this is really malaria – of we might not.

A positive "Widal" test does not necessarily show current typhoid infection: It is the demonstration of actively rising titres that shows an active typhoid infection.

Definition: The predictive value of a measurement is the probability that those it shows as having a particular condition actually have it.
It has two components:

1. Positive predictive value: The proportion of those who test positive that in reality has the disease (probability that a person has disease, given that he/she tests positive)

2. Negative predictive value: The proportion of those who test negative that in reality does not have the disease (probability that a person has no disease, given that he/she tests negative)

Assessing predictive value of a test: The assessment of predictive value is converse to the assessment of sensitivity and specificity. We obtain a representative sample of the population, whom we test first with the less accurate 'Screening Test'. This dives the sample into two – those who the 'Screening Tests' shows positive results and those whom it does not. Thereafter, we apply the 'Gold Standard' to determine the proportion among those who test positive with the less accurate screening test that actually have the condition of interest and the proportion of those who test negative that in reality do not have the condition of interest.

The 2X2 table for predictive value

		Disease Status		
Test Result		**With Disease**	**Without Disease**	
	+ve	a (TP)	b (FP)	(a+b) or (TP + FP)
	-ve	c (FN)	d (TN)	(c+d) or (FN + TN)
		(a+c) or (TP+ FN)	(b+d) or (FP + TN)	(a+b+c+d)

TP= True Positives; FP= False Positives; FN= False Negatives; TN= True Negatives

Positive Predictive Value (PPV) = $\frac{TP}{TP + FP}$ or $\frac{a}{(a+b)}$

Negative Predictive Value (NPV) = $\frac{TN}{FN + TN}$ or $\frac{d}{(c+d)}$

Relationship between predictive value and Prevalence: Unlike sensitivity and specificity that apply directly to the inherent properties of a test, the predictive value of a test is affected by two factors:

1) Prevalence of the Disease in a population
2) Specificity of the test

Example 2.2.4: Predictive Value and Prevalence

Scenario 1: Population with low prevalence of malaria

Population 1: 10,000pple
Test used: Sensitivity: 90%
Specificity: 90%
Disease: Malaria
Prevalence: 1% therefore expected diseased are: 100

When we use the information above to calculate the different categories and fill a 2X2 table, we obtain the following information:

True Characteristics in the population

Results of screening	**Disease**	**No Disease**	**Total**
Positive	90	990	1080
Negative	10	8910	8920
Total	100	9900	10,000

Therefore: **PPV** = 90/1080 X 100 = 8.3% **NOTE!**

NPV = 8910/8920 X 100 = 99.8%

Scenario 2: Population with higher prevalence of malaria

Population 1: 10,000pple
Test used: Sensitivity: 90%
Specificity: 90%
Disease: Malaria
Prevalence: 10% therefore expected diseased are: 1000

True Characteristics in the population

Results of screening	**Disease**	**No Disease**	**Total**
Positive	900	810	1710
Negative	100	8190	8290
Total	1000	9000	10,000

Therefore: **PPV** = 900/1710 X 100 = 52.6%: **NOTE!**

NPV = 8190/8290 X 100 = 98.8%

Deduction

A 9% difference in prevalence led to a 40% difference in the positive predictive value of the test. Therefore, at low prevalence of disease, a change in prevalence significantly affects the positive predictive value of a screening test; NPV is does not change significantly. With diseases of high prevalence, the same is true for negative predictive value

Application

1. A screening programme is more effective if applied to a high risk population: screening for syphilis would be more predictive of the actual situation is applied to prostitutes than to celibate monks

2. The results of any test must be interpreted in the context of the prevalence of the disease in a population: *In Uganda every one with a fever has malaria unless proved otherwise – High Positive predictive value because malaria is highly endemic; in the United States, this assertion would be very wrong*

Relationship between predictive value and specificity: Predictive value of a test increases with specificity of the test; the same may not be demonstrated for sensitivity.

d. Reliability of measurements

Reliability is synonymous with Repeatability: Reliability is related to the consistency of a measurement technique. When the same measurement is repeated many times and the same result is obtained all the time, then the test is said to be reliable. For example, if a weighing scale measures the same object many times and it records the same weight all the time then that scale is reliable. If each result is different from the others then the scale has got low reliability. Reliability therefore is concerned simply with the repeatability of measurement. It is important, however, to note that reliability alone does not necessarily indicate validity. To appreciate this better, please read about precision and accuracy. While these definitions are apparently easy to understand, the dilemma in real life is how to obtain the "truth" so as to assess how far the result differs from the correct situation. The factors that contribute to the difference between the result and the correct situation include intrasubject variation, intra-observer variation and interobserver variation. These are briefly discussed.

1. Intrasubject Variation

The values obtained in measuring many human characteristics often vary over time, even during a short period. For example: Changes in blood pressure readings over a 24-hour period in three individuals are illustrated in the table below:

Table 1.9

Blood pressure (mm Hg)	Female Aged 27 yr	Female Aged 62 yr	Male Aged 33 yr
Basal	110/70	132/82	152/109
Lowest hour	86/47	102/61	123/78
Highest hour	126/79	172/94	153/107
Casual	108/64	155/93	157/109

Variability over time is considerable. These, as well as the conditions under certain tests are conducted (e.g. post-exercise, post-prandially, at home or in a physician's office), clearly can lead to different results in the same individual. Therefore in evaluating any test result, it is important to consider the conditions under which the test was performed, including the time of day.

2. Intra-observer Variation

Values of two or more readings of the same test results by the same observer can vary. The degree of intra-observer variation in the readings depends on the influence of the subjective factors.

For example: A single ultrasonographer conducted transvaginal scans using an ultrasound machine to diagnose for polycystic ovarian syndrome among 27 women. Using a Panasonic video-editing system, the 27 scans were duplicated giving a total of 54 ultrasonographic records. Each record was given a number and arranged randomly in a final edited videotape recording. Four experienced observers in transvaginal ultrasonography evaluated the videotape recording and were asked to score the appearance of each ovary and these were findings:

Observer	Intra-observer agreement/variability (n=27)
1	20, 74%
2	21, 78%
3	17, 63%
4	17, 63%
Overall	**69.4%**

Source: Amer, Bygrave, Sprigg et al. An evaluation of the inter-observer and intra-observer variability of the ultrasound diagnosis of polycystic ovaries. Hum Reprod (2002) 17 (6): 1616-1622.

3. Inter-observer variation

Another important consideration is variation between observers. Two examiners often do not derive the same result. The extent to which observers agree or disagree is an important issue whether we are considering physical examinations, laboratory tests or other means of assessing human characteristics. We therefore need to be able to express the extent of agreement in quantitative terms.

Percent Agreement

In determining Percentage Agreement, we obtain a sample of the population. We subject them to tests by the first observer, who reports those he/she determines to have the condition and those who do not have. We then subject them to the second observer. These findings can be represented in a 2X2 table as follows:

		Observer 1		
Observer 2		+Ve	-Ve	
	+Ve	a	b	
	-Ve	c	d	
				a+b+c+d

Percent Agreement is then computed as the proportion of tests for which the two observers agree, ie.

$$\frac{a+d}{a+b+c+d} \times 100$$

Refer to Leon Gordis to find more information about the **Kappa Statistic.** This concept will be covered in Applied Epidemiology II

Further Reading

Leon Gordis: Epidemiology, 3rd Edition, Chapter 4
Foundations of Epidemiology 3rd edition by Lilienfeld and Stolley chapter6, p117-128.
Basic Epidemiology by Beaglehole et al. Published by WHO 1993.

Exercise 2.2.5: Public Health application of validity

In your discussion groups of two, please go through the exercises on **application of validity** from, CDC – Epidemiology Programme Office: Case studies in applied epidemiology No. 871-703. **Screening for antibody to HIV** – Students' Guide. It will not only help you understand the calculations of validity and their variations with predictive value, but it will also demonstrate the context in which validity becomes an extremely important tool in public health interventions. You can also download it from: www.cdc.gov/eis/casestudies/XscreeningHIV.student.871-703.pdf

Session 4: Disease Surveillance

Introduction: In order to detect abnormal patterns of health-related events, epidemiologists often set up long term mechanisms for tracking of diseases. While short term surveys assess the magnitude of health-related events at a point in time, surveillance allows us to continually track these events over time. This enables us to assess 'trends in the incidence and prevalence of these events over time'. This is called surveillance. Surveillance is one of the core functions in epidemiology and disease control. This session provides an initial overview of the principles of surveillance. A more detailed discussion of the applications of surveillance in disease control is presented in another course on Surveillance.

Lesson Outline:

a. Principles of disease surveillance
b. Types of Surveillance
c. Key requirements for a surveillance system
d. Setting up a surveillance system
e. Overview of the IDSR strategy in Uganda

Lesson Objectives:

By the end of this lesson, the student should be equipped with the competency to:

1. Relate the principles of disease surveillance to routine management of health services
2. Describe the types of surveillance and the situations in which they are desired
3. Describe the rationale and components of the Integrated Disease Surveillance and Reporting (IDSR) strategy

a. Principles of Disease surveillance

Definition of surveillance: It is the on-going systematic collection, collation, analysis and interpretation of data, and the dissemination of information to those who need to know in order for action to be taken.

Rationale for disease surveillance: In order to detect unusual increases in the trends of disease, we need methods and systems for tracking disease frequency over time. Otherwise, cross-sectional data may not be sufficient to tell us if indeed the incidence or prevalence of a particular condition is increasing or not. For rare diseases or diseases that are not expected to be prevalent, surveillance helps us to detect them at the earliest time point at which they occur or increase so that appropriate disease control actions are undertaken before the situation develops into an epidemic.

How do we decide which health conditions to conduct surveillance for? For a particular disease, we are interested in the following issues:

- What is its public health importance?
- Can public health action be taken?
- Is relevant data available?
- Is it worth the effort in terms of resources committed to controlling it?

Objectives of surveillance: Surveillance is important in

- Epidemic (outbreak) detection

- Epidemic(outbreak) prediction
- Monitoring trends in endemic disease
- Evaluating interventions
- Monitoring progress towards control
- Monitoring programme performance
- Estimating future disease impact

b. Types of Surveillance

- Active Surveillance
    - Case-Based Surveillance
    - Case-Based Laboratory Backed Surveillance
- Passive Surveillance
- Sentinel Surveillance
- Community Surveillance
- Risk-based surveillance

Passive Surveillance: In passive surveillance, health authorities at higher administrative levels wait for the lower level units to provide the surveillance reportse.g. in Uganda, the Health sub-districts and districts often wait for the lower health facilities to provide the monthly Health Management Information System (HMIS) reports.

- What do you think are the advantages of passive surveillance? What are the disadvantages?

Active Surveillance: Active surveillance is a more aggressive form of surveillance that involves health officials at the administrative levels going down to the operational levels (e.g. health facilities and other sources of data on disease events) and soliciting for information/reports in health related events. Active surveillance is usually focused on diseases of higher public health concern e.g. diseases targeted for elimination/eradication; epidemic prone diseases. Active surveillance includes 'Case-based surveillance' and 'Case-based Laboratory-backed surveillance'.

- **Case-Based Surveillance:** It involves rigorous investigation of each case that occurs. Whenever a suspected case is reported, we conduct detailed investigation of the case, its contacts and the events surrounding the case. Polio and Meningitis are examples diseases for which we conduct detailed surveillance activities
- **Case-Based Laboratory Backed Surveillance:** This refers to case-based surveillance in which the investigative rigor includes conducting one or more laboratory tests to confirm/rule out disease presence of affirm cure from the disease. It is often necessary for some diseases for which clinical features are insufficient to support a confirmatory diagnosis due to the condition having many differential diagnoses. It is often done for diseases that are targeted for eradication/elimination.

Sentinel Surveillance: In sentinel surveillance, surveillance for a particular disease is not conducted in all health care facilities but we select specific sites where surveillance for particular diseases is conducted. This is usually due to the nature of the disease and the complexity in tracking it (e.g. Surveillance for HIV/STDs in the sexually active population may be conducted in selected health facilities where all women seeking antenatal care undergo HIV and Syphilis screening; Surveillance for Chronic Obstructive Pulmonary Disease (COPD) is best conducted in regional and national referral hospitals because this condition requires a high level of experts to collate information from different tests in order to make a diagnosis of this condition.

Community Surveillance: In community surveillance, communities are actively involved in finding of new or prevalent cases.

Risk-based surveillance: This type of surveillance is mainly for the emerging pandemic threats. Many of these threats arise from human interactions with animals in areas that at high risk. It involves setting up passive and active surveillance systems but in specific areas that are at high risk – high risk populations; high risk pathogens; high risk geographic hot-spots; and high risk animal species. These concepts will be explored more in the courses on Disease Surveillance and Communicable and non-Communicable Disease control

[Refer to the Presentation: 'Principles of Surveillance' in your additional resources folder for further notes on the types of surveillance]

c. Key requirements for a surveillance system

Surveillance indicators: Should be specific, measurable, action oriented, realistic and time bound. Indicators should be selected on the basis that they are sensitive enough to detect the relevant event.

Surveillance data: In surveillance, we collect information on particular health related events that may be diseases (e.g. Measles case based surveillance), syndromes (e.g. Jaundice, AFP), public health issues, public health issues (e.g. Infant Mortality Rates) or the environment (e.g. vectors and water contamination).

Sources of data: There are several sources of data and information that include: The Health management information system (HMIS), vital statistics records, surveys and laboratory.

Case definitions: To facilitate the detection of cases, we often have case definition. These include several criteria that may be clinical, laboratory or a combination. Depending on the disease, we have different levels of affirmation that include suspected, probable and confirmed cases. These case definitions can then be developed into indicators or thresholds for predicting possible outbreaks.

Activity 2.2.8: Contact the disease surveillance focal person in your District Health Office and obtain a copy of priority notifiable diseases. Read through to acquaint yourself with these case definitions.

Reporting: The frequency of reporting depends on the urgency with which information is required. It may be immediate (especially for diseases whose outbreak threshold is one case), weekly (for notifiable diseases), monthly (e.g. the health unit monthly reports), quarterly (e.g. the HSD quarterly assessment reports. Three important parameters in reporting are timeliness, completeness and accuracy.

Activity 2.2.9: Contact the HMIS Focal Person in your District Health Office and obtain a copy of the Health Management Information System. Read through and acquaint yourself with the different types of reports and their scheduling.

Reporting methods: Several communication channels can be used, including paper reports, e-mail, courier and telephone.

Surveillance data flow: Information flows from peripheral levels (communities, lower level health centres) to Intermediate levels (HSDs and Districts). Intermediate levels may provide supportive laboratory data and demonstrate a probable epidemiological link. Information then flows to the centre (Ministry of health) and subsequently to the regional and international levels (Country coordinating teams, WHO and other bilateral/multilateral agencies).

Analysis and interpretation: It is very important that data is analysed and interpreted in order to inform action. Analysis includes examining the data to assess validity in terms of timeliness, completeness and accuracy. Data validation involves making a descriptive analysis to describe the characteristics of the affected populations in terms of who is affected, when and where (time, place and person).Descriptive information enables us to generate hypotheses.

Action: It involves control of events (e.g. outbreaks), preparedness and feedback. It also involves policy reformulation and evaluation of interventions as well as the surveillance system itself

d. Setting up a surveillance system

Criteria for identifying priority health events for surveillance: A number of criteria may be used that include:

- Frequency of the event (incidence, prevalence, mortality)
- Severity (Case fatality, hospitalisation rates and disability rates)
- Cost (Direct and Indirect costs)
- Preventability and communicability
- Public Interest

Steps in planning a surveillance system

- Establish objectives
- Develop case definitions
- Determine data source or data collection mechanism (type of system)
- Develop the data collection instruments
- Field test the methods
- Develop and test analytical approach
- Develop dissemination mechanisms

Attributes of a good surveillance system: Qualitative attributes of a good surveillance system include: Simplicity, flexibility, acceptability. Quantitative attributes include sensitivity, predictive value, reliability and representativeness as well as timeliness and cost effectiveness.

e. Overview of the IDSR strategy in Uganda

Uganda implements a policy of integrated disease surveillance that started way back in 2000. Implementation was preceded by an assessment of the surveillance systems and their performance in March 2000. Priority diseases included in the IDSR in Uganda are shown in the table below:

Diseases targeted for eradication/Elimination	Epidemic prone diseases	Diseases of Public health importance
AFP/Polio Guinea worm Leprosy Maternal/Neonatal tetanus (MNT)	Cholera Dysentery Measles Meningococcal Meningitis Plague Rabies Viral Hemorrhagic fever Yellow fever	HIV/AIDS Injuries Malaria Onchocerciasis Pneumonia in under 5s Schistosomiasis STI Trypanosomiasis Tuberculosis Typhoid fever

Organisation of IDSR in Uganda: Coordination is done by an IDSR committee that meets regularly and represents all stakeholders. The Epidemiological surveillance division (ESD) in the Ministry of health is the liaison office for IDSR. Notifiable diseases are reported to the ESD immediately (within 24 to 48 hours) using telephone, radio-call and e-mail. They are also reported on a weekly basis using the HMIS notifiable diseases report. Reports include cases and deaths. The division monitors the trends and publishes a weekly news letter on the state on notifiable diseases in the country. Case based surveillance has also been put in place especially for measles, TB and AFP. Case based reporting is channelled to the line programmes (Expanded Programme on Immunisation, Uganda Guinea Worm Eradication Programme, and the AIDS Control Programme).

Surveillance methods: Mainly passive case detection at the peripheral health units and communities. For selected diseases, there is active surveillance in which any suspected case is fully investigated, characterised and followed up. These include measles and AFP. For some diseases, especially in which it is hard to fully characterise the incident cases, sentinel surveillance sites have been set up (e.g. HIV sero-surveillance is conducted at about 7 sentinel sites spread across the country. Pregnant women attending antenatal are taken as the reference population. There is also case based surveillance for selected diseases targeted for eradication or elimination.

Case Based Surveillance for Measles

Measles is a disease that has been targeted for eradication in Uganda. According to the Expanded Programme on Immunisation, 4 strategies have been taken for the elimination of mortality and reduction of morbidity due to measles in Uganda:

1. Improve coverage and quality of routine immunisation
2. Ensure a second opportunity for measles immunisation (routine or supplemental)
3. Establish an effective surveillance system
4. Improve case management and provide Vitamin A supplementation.

Mass campaigns have been conducted country-wide in addition to strengthening routine immunisation. More-over, catch–up campaigns have been conducted in between the mass campaigns and follow up campaigns have been planned, especially for the older age groups and those infants that were left out in the earlier campaigns.

As a result, measles outbreaks that were a common feature have dwindled. Moreover, the age group affected has tended to 'shift to the older groups'. However, there are still cases presenting with the defining symptoms of measles, which necessitated the establishment of case based surveillance. The defining criteria for **suspicion** of measles are: *A child with cough, coryza and conjunctivitis, preceded by a fever and followed by a rash.* The epidemic threshold for measles is 3 cases per parish per week or 25 cases per 100,000 populations or 1 case in a crowded settlement e.g. a refugee camp. For a post campaign period, the threshold is defined as "a cluster of 5 or more suspected cases or at least 3 IgM positive cases in a catchment area of a health facility in a month.

In case of no epidemic, all these cases are investigated and blood samples taken and sent to the Uganda Virus Research Institute (UVRI) Laboratories within 48 hours. In normal situations, health workers are required to draw blood samples and take them directly to UVRI, which tests the samples and posts a feed-back. This process is called **case-based laboratory backed surveillance**. They are then facilitated with a transport refund and lunch. It has been observed that the majority of suspected measles cases in fact turn out to be other non-specific viral rashes

and especially rubella. NB.

In measles outbreaks, case based – laboratory backed surveillance is abandoned and replaced with case based line-listing and management of incident cases as well as health education. Mass immunisation is already too late in such settings, but can be targeted for the adjacent parishes with a low routine coverage. In the affected parish, we mainly concentrate on case management, and strengthening routine immunisation.

Activity 2.2.10a: Please read about case based surveillance for measles, Guinea worm and AFP.

- What do you understand by case based surveillance?
- Why is case-based surveillance important in measles control?
- What are the important activities in measles case based surveillance?
- How is a measles outbreak handled?

Activity 2.2.10b: Please read the manual titled: ***"UNEPI – Disease surveillance manual"*** for an in-depth understanding of the surveillance for priority immunisable diseases in Uganda.

EXERCISE 2.2.6: Exercises on disease surveillance

For your personal practice, please go through the exercise contained in the **additional resources** folder, named **exercises on disease surveillance.** It will give you a feel of what is involved in the use of surveillance systems to detect diseases of public health importance.

Information flow in IDSR: Information flows from the health units to the Surveillance focal person and the HMIS focal person at the district level. It is then sent to the centre. The centre then makes a feedback to the districts on timeliness, completeness and accuracy of the information.

Progress in IDSR implementation in Uganda: The WHO/AFRO generic guidelines for IDSR were adopted. Standardised case definitions have been developed and reporting formats circulated. Laboratory focal persons have been identified at district level

Session 6: Outbreaks and Outbreak Investigation

Introduction: Epidemics are one of the most important events in epidemiology. The dramatic nature of these events has the potential to stretch disease control efforts, leading to a high loss of life and a disruption of health service delivery. In this session, we discuss some principles of outbreaks and outbreak investigation.

Lesson Outline:

a. Detection of outbreaks
b. Steps in outbreak investigation
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Lesson Objectives:

By the end of this lesson, the student should be equipped with the competency to:

1. Define key terms related to disease outbreaks
2. Distinguish the different types of outbreaks
3. Describe the tasks involved in the investigation of an outbreak

a. Outbreaks

Definition: An outbreak is the occurrence of a disease or event in excess of what is expected in terms of persons, place and time.

Detecting an outbreak: As noted above, we can detect an outbreak by assessing if an event is occurring in excess of what is expected for a particular population (person), locality (place) and over a given period of time (time). The key questions therefore are:

1. Who is affected? (Person)
2. When? (Place)
3. Where? (Time)

Reflection:
List some of the key outbreaks that have occurred in your locality in the last decade

Important considerations in detection of outbreaks:

- There ought to be a case definition for known diseases. For unknown (strange/new) diseases there ought to be a 'working case definition'
- Un-expected rise in new cases
- The rise exceeds a threshold
- Thresholds differ from disease to disease, for example:
    - Cholera – One confirmed case
    - Ebola – One suspected case
    - Measles – 3 cases from one parish in a week or 25 cases occurring in a 'HSD'
    - Meningococcal Meningitis – 10 cases in a district in a higher risk country/region (meningitis belt) or 5 cases in a lower risk country/region
    - STDs – Sudden or insidious rise in prevalence beyond the usual/seasonal trends
    - Malaria – Sudden or insidious rise in prevalence beyond the usual/seasonal trends

Determinants of Outbreaks: The amount of disease in a community depends on the balance between the proportion of the population that is *susceptible*, and that which is *immune.* Disease is

propagated if susceptible people get into contact with infected people. If the balance between immunity and susceptibility is towards susceptibility, there is an increased likelihood of an epidemic. If the balance is in favour of immunity, then there will be *herd immunity* and the likelihood of an epidemic is low.

Epidemic, pandemic and endemicity: An outbreak in a locality is an epidemic. A wide spread epidemic at multiple localities across the globe is a pandemic. A disease that exists at more or less constant levels of prevalence in a community is described as endemic. Depending on the level of prevalence, a disease may be described as Holo-endemic, hyper-endemic, meso-endemic or hypo-endemic.

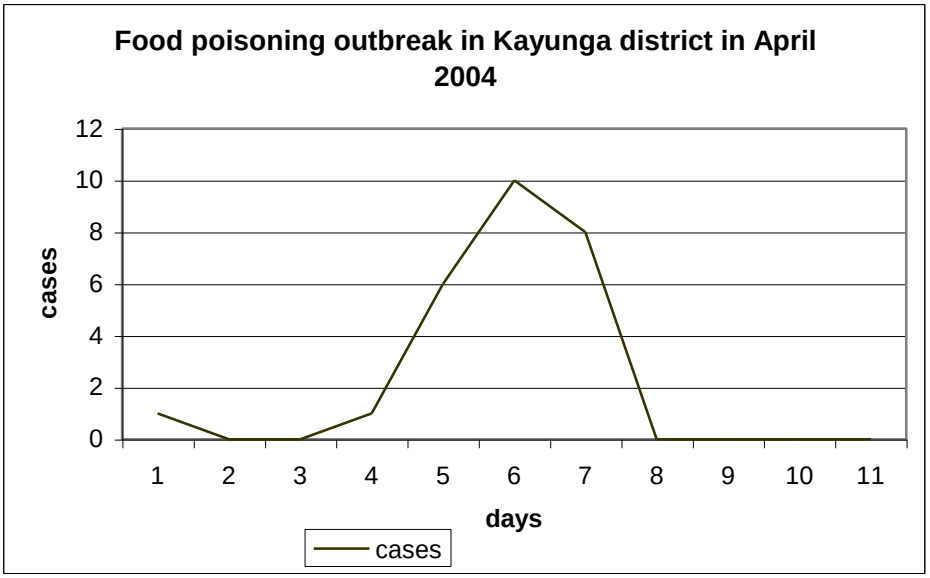
The incubation period: Three critical questions in investigating an outbreak are:

-When did the exposure begin?
-When did the disease begin?
-What was the incubation period of the disease?

If any two of the three are known, the third can be calculated.
The incubation period is the time interval between invasion by an infectious agent and appearance of the first sign and symptom of the disease in question. In a **vector**, it is the period between entry of the infectious agent into the vector and the time at which the vector becomes infective
The epidemic curve: To detect and characterise an outbreak, we often make a plot of cases over time. This is known as the epidemic curve. Time may be a direct expression or a transformation into the logarithmic function (Log – time).

Examples of epidemic curves - The Kayunga outbreak: In April 2004, there was an outbreak of a disease that caused abdominal pains, diarrhoea and vomiting in Kayunga District in Uganda. At the time, there were wide spread sporadic outbreaks of cholera in the country, and it was thought this was part of the pattern. Further investigation revealed that two people had died after consuming some left over potatoes at a funeral. Thereafter, there was a rapid increase in cases. All cases reported having attended the funeral, or having partaken of the ill-fated meal of potatoes. In Kayunga, there is a tribe of in-migrants of Sudanese origin who conduct protracted funeral ceremonies spanning several weeks. The outbreak was characterised as a single exposure – common vehicle outbreak. A plot of cases over time showed the classical epidemic curve for such outbreaks as is shown in the graph below:

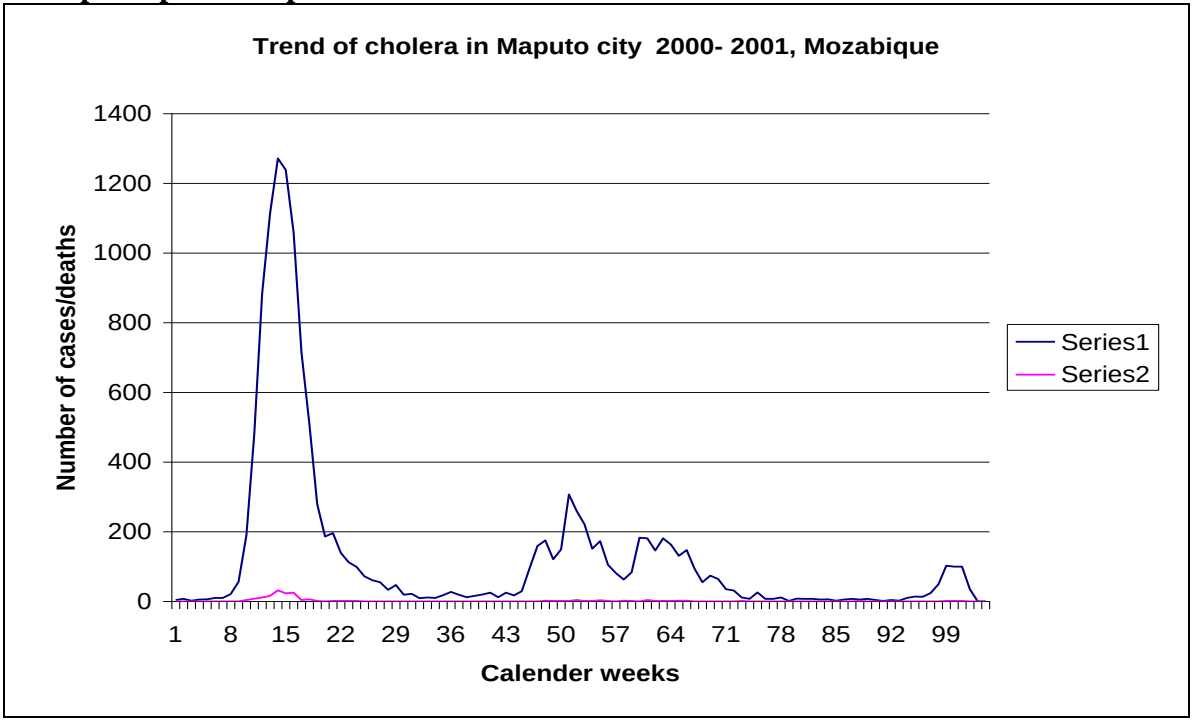
Single exposure – common vehicle epidemic curve



Notes: In a single exposure – common vehicle epidemic, the curve represents the distribution of the incubation periods. In the first few hours, or days (depending on the incubation period) there is a sharp rise in cases, till a peak, and subsequently, a reduction in incident cases.

Example 2.2.5: Worked example on a Food-poisoning outbreak in Kayunga
To read more about this outbreak, please refer to the **additional resources** folder. It will help you appreciate the unique features of a single exposure – common vehicle epidemic, of which food borne outbreaks are a classic example.

Multiple exposures epidemic curve



Notes: In a multiple exposure epidemic, the curve shows more than one peak. The different peaks indicate secondary attacks. This often occurs where there in a vehicle or vector that continuously or periodically propagates the process of disease transmission.

Terms: The following terms are important in characterising an outbreak:

Common vehicle exposure: There is a point source of exposure which all cases share. This is common in food poisoning outbreaks, where an infested meal is served for lunch to a number of mourners at a funeral.
Single exposure: There in only one round of exposure from the point source e.g. the above meal is served only once.
Multiple exposures: There is more than one round of exposure from the point source e.g. the left over portion of the above meal is again served for supper
Periodic exposure: There is a contaminating source that introduces infestation intermittently e.g. a leaking sewerage pipe may contaminate a water source in the rainy season but not in the dry season.
Continuous exposure: There is continuous contamination of the utility, not varying in time.

Single exposure common vehicle outbreaks: These outbreaks are often easier to characterise. They are explosive, with a rapid increase in the number of cases in a population. They are limited to people who share a common exposure. Secondary cases rarely occur. An example is the food-borne outbreaks.
Multiple exposures epidemics: In such outbreaks, there is a factor (vehicle or vector) that propagates the transmission process. In such outbreaks, the person who acquires the disease form the initial source is the *primary case.* The person who acquires the disease from a primary case is the *secondary case*

Measuring outbreaks: In measuring outbreaks we may use a special form of incidence rate – the ***attack rate.*** It is similar to the incidence rate, except that the time is expressed implicitly.

Attack rate =

$$\frac{\text{Number of new cases of a particular condition}}{\text{Population at risk}} \times 100$$

The attack rate can be specific for a particular exposure: e.g.:

Food specific attack rate:

$$\frac{\text{Number of people who ate a certain food and became ill}}{\text{Number of people who ate that food}} \times 100$$

In multiple exposure or propagated epidemics, there are different attack rates for each episode of exposure. These are described as secondary attack rates

b. Steps in investigating an outbreak

The following steps are important in outbreak investigation and control. They are not exactly sequential or hierarchical – some of the steps can be done concurrently.

Step 1: Obtain initial notification of the outbreak

We receive information about the likelihood of an outbreak from surveillance systems (passive and active), Information and reporting systems (Health Management Information System), Clinicians and Nurses in health units, Community resource persons (leaders, village health teams, parish development committees). Every rumour must be investigated!

Step 2: Initial response

Assemble team and prepare for an initial field visit as soon as possible. Assemble the immediate necessary logistics including fuel, transport, supplies and equipment and alert the district authorities.

Step 3: Verify diagnosis

Review the clinical findings: visit the patients, interview, examine, and reassure them. Take samples for laboratory confirmation as soon as possible. Choose a working case definition that is sensitive enough to detect the cases of interest. Establish the index case.

Step 4: Confirm the existence of an outbreak

Compare the observed incidence with the expected, and relate to seasonality. Use the action threshold in the case definition to confirm the existence of an outbreak.

Step 5: Identify and count cases

Use the working case definition to line-list all cases, starting with the index case. Collect additional information on demographic characteristics (age, sex, and tribe), date of onset, and outcome (death, or cure), complications and exposure risk factors.

Step 6: Assess the local response

Establish a district level task force and allocate them their responsibilities, including community mobilisation and IEC. The task force may include politicians, civil society organisations and the DHT. Ascertain the number and type of personnel as well as logistics available for case management (drugs, medical supplies, guidelines).

Step 7: Set up immediate control measures

Treat cases, to interrupt transmission and reduce mortality/complications. Consider vaccination, chemoprophylaxis, health education, disinfection and use of protective wear, depending on the infectivity of the agent causing the outbreak. To interrupt transmission, assess the epidemiological triad and trace the risk factors.

Step 8: Address the resource gaps.

This depends on the nature and extent of the outbreak, as well as the capacity at the district. Resources may be needed in the areas of laboratory support, IEC, and specific infection control needs like JIK, protective wear and vaccines.

Step 9: Describe the Outbreak

Using available information, analyse data to establish the exposure risk factors. Define the numerator (the cases) and the denominator (population at risk). **Who** is affected? **When** and **Where**? We can also pose the question – why, how and what? Use appropriate tools to display the

data (graphs, spot maps etc.). Determine the size of the population at risk, using spatial and temporal criteria and relating them to how the disease in spread. Calculate the attack rates and case fatality rates.

Step 10: Formulate and test hypothesis
Formulate a hypothesis on the source of the event, its transmission, the causative agent, and the exposure risk factors. We also look for combinations or interactions of various factors. We can conduct analytical studies (especially case control) to ascertain this.

Step 11: Report writing and dissemination
Prepare a report describing the situation using the experiences and answers you have obtained. Recommend priorities and control measures to be addressed and make deductions on the outbreak. Disseminate your findings to those who need to know and act (Ministry of health, the DHT and the District Local Council). Disseminate to the community, especially through their leaders (Village and Sub-county health teams, parish development committees etc).

Step 12: Be on your guard: Strengthen your surveillance system
Maintain daily updates on the outbreak to assess whether it is under control. Maintain a robust records system, and analyse data to establish trends. Establish measures to ensure that the same outbreak does not happen in future.

EXERCISE 2.2.7: Exercises on outbreak investigation

For your personal practice, please go through the exercise contained in the **additional resources** folder, named **exercises on outbreak investigation.** It will give you a feel of what is involved in the detection and investigation of outbreaks for diseases of public health significance.

Lesson 6: Descriptive Epidemiological Study Designs

Introduction: Observational studies are divided into descriptive and analytical study designs. Descriptive studies are often the starting point of epidemiological inquiry. They are used to describe initial patterns of the relationship between exposure and disease, to discern possible associated factors. They are therefore very useful in setting hypotheses, as the basis for further analytical studies.

Lesson Topics: In this lesson, you will cover the following topics:

a. Case series and ecological studies
b. Cross-sectional studies

Lesson Objectives:
By the end of this lesson, the MPH student should be able to

- Design and conduct Case series and Ecological studies
- Design and conduct Cross-sectional studies.

a. Case Series and Ecological Studies
Please read about **Case series** and **Ecological** studies. ***Case series*** are descriptive study designs in which a series of similar cases is described. Observation of abnormal patterns often starts with observation of an unusual case, followed by a case series. It is from these series that an opinion is made that there is an abnormality to be investigated.

Example 1: A surgeon realises that all the cases with lung cancer under his care are cigarette smokers.
Example 2: An ophthalmologist realises that all new-borns with an unusual form of cataract were born to mothers who had rubella when pregnant.

Since there is no comparison group, we cannot directly infer causality. However, the background information can enable us to formulate a hypothesis, which can then be tested using analytical studies.

Ecological studies are epidemiology studies that focus on comparison of groups of people or populations rather than individuals. They explore potential associations between one or more population level exposures and outcomes when alternative study designs are not applicable. They generate hypotheses of potential exposures of an outcome. However, inferring population characteristics to causation is dangerous: If there is a high incidence of breast cancer in Sweden and people in Sweden tend to take on average a lot of fat in their diet – can we conclude that taking a lot of dietary fat causes breast cancer? This dilemma is what has been described **Ecological fallacy** (please read more about it).

Design and analysis of ecological studies: This involves collecting group level data e.g. Country, state, city etc on exposures (population risk- and confounding factors) and outcomes (disease incidence or prevalence). The measure of association is the correlation coefficient – r, demonstrates the relationship between the exposure and outcome.

The different types of ecological studies include:

- Multiple group study

    - Involves comparing an outcome across groups or geographical areas like regions or countries during the same period.
- Time-trend study
    - Comparing outcome rates over time in one population
- Mixed design
    - Multiple groups and multiple time periods

Reasons for conducting ecological studies include:

- If group level data on exposures is available
- Comparison of data across geographical or regional units is feasible and inexpensive
- If ecological effects are of interest in the study
- Data analysis and presentation are simple
- Measurements of some exposures or outcomes may be difficult at individual level

Advantages of ecological studies: They are easy and quick to conduct. They are inexpensive. They can address research questions that cannot be answered by other observational study designs at individual level. They allow estimation of effects not easily measurable at individual level. They permits exploratory analyses of potential factors in disease aetiology – generating hypotheses.

Disadvantages of ecological studies: It is difficult to link the outcome to exposure in individuals. They are prone to ecological fallacy – error that occurs when findings from an ecological study are used to draw conclusions at an individual level. It is difficult to control for confounding due to lack of data on all potential confounders. No correlation may not mean a lack of association between exposure and disease. They may generate false positive or negative associations. The "average" exposure level is assessed- this does not represent individual levels and may mask dose-response relationships. Collinearity may occur and this entangles the effects of the predictors thus complicating interpretation of findings. They are commonly dependent on data that has been collected for other purposes (Please read more about this study design).

b. Cross-sectional Studies

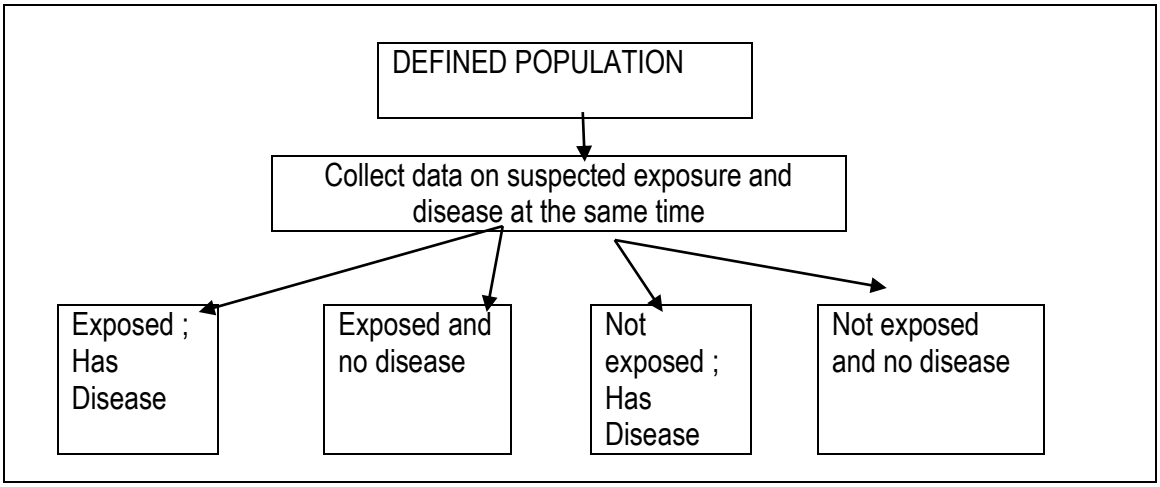
Cross-sectional studies are mainly used for examining the characteristics of populations so as to detect associations with events of interest. They study the population at a particular point in time and therefore may not be used to infer causality. However, they provide an insight into important associations between several factors and a particular event, or several events and a particular factor. They may be the basis for formulating hypotheses that may lead to further investigations using analytical studies or experiments.

Characteristics of cross-sectional studies:

- They are conducted a single point in time or over a short period
- There is no follow-up
- They take a snapshot look at the population
- They are often called prevalence studies because it ascertains prevalence of exposures and outcomes; often times they are called 'surveys' although the term 'survey' carries a broader meaning.

Design of a Cross-sectional study: The relationship between exposure and disease is assessed simultaneously e.g., we may want to associate high cholesterol levels to increased risk of Congenital Heart Disease. In this case, we assess for congenital heart disease and cholesterol

level at the same time. For this reason, Cross-sectional studies are often referred to as prevalence studies.



Analysis of cross-sectional studies:
Cross-sectional studies mainly generate descriptive information. The primary objective is not comparison but description. To summarize the descriptive status of the population we mainly report on:

- Means, modes, medians for numerical data
- Frequencies and Rates/Ratios/Proportions for categorical data

We then formulate hypotheses that can be tested in analytical studies

In the analysis of cross-sectional studies, we can also conduct comparisons between our 'presumed' outcome factor and the 'exposure' factors:

- The outcome of interest and the factors that may be associated with that outcome are assessed at the same point in time
- We can compare prevalence of 'disease' in exposed & non-exposed
- We can also compare the prevalence of exposure in those with 'disease' and those without

We can represent the findings in a 2X2 table if the outcome is dichotomous:

		First select		
Follow up past exposure		**With Disease**	**With no disease**	
	Have exposure	a	b	(a+b)
	Have no exposure	c	d	(c+d)
		(a+c)	(b+d)	(a+b+c+d)

In analyzing such findings with a dichotomous outcome we may calculate:

i) The prevalence of disease in persons with a suspected exposure **(a/(a+b))** and compare with the prevalence of disease in persons without exposure **(c/(c+d))**.
j) We can also calculate the prevalence of the suspected exposure in persons with the disease **(a/ (a+c))** and compare with the prevalence of exposure in persons without the disease **(b/(b+d))**

Importance of cross-sectional studies: Cross-sectional studies are the most frequent quantitative study conducted in epidemiology. They are quick and relatively cheap to implement.
Challenges of cross-sectional studies: The main challenge of cross-sectional studies is that they assess both the suspected exposure and outcome at the same time. They are therefore not suitable for determining causality as a temporal relationship between the proposed exposures and the outcome cannot be demonstrated.

Cross-sectional studies identify prevalent other than incident disease. If there is an association therefore, it is more related to survival with the disease. In addition, it is not possible to establish a temporal relationship – we cannot tell what preceded the other: the heart disease or the cholesterol.

What other challenges you think might arise from cross-sectional studies?

Areas for Further Reading
Read about special types of cross-sectional studies called 'ecological studies' or 'correlational studies' and try to understand what is meant by the term 'ecological fallacy'.

2.2.7 Extension Activities

Extension Activity 1: Discussion Forum Question
Descriptive Epidemiology covers several areas that include: Measurement of Disease, Standardisation of Rates, Validity and Reliability of Measurements, Principles of Disease Surveillance and Outbreaks and Descriptive Study designs; For this forum, we shall focus on validity of measurements – Briefly Describe some measures of validity and how they can be applied to selection of screening tests for different purposes

Extension Activity 2: Self- Assessment Quiz

QUIZ 2.2.1
(Select the most correct option)

1. A rate is characterised by all of the following except
    a. It is a proportion that includes a specification of time
    b. It refers to instantaneous change in one quantity per unit change in another
    c. Maternal Mortality Ratio is a classic example
    d. The numerator is always part of the denominator
    e. None of the above

In a school of 300 students, the number of people that developed diarrhoea during the first 3 months of 1999 was as follows: January 10 cases, February 6 cases and March, 14 cases. Use this information to answer question 2 and 3.

2. It can be said about the above school that:
    a. The prevalence is 30 cases
    b. The prevalence is 10 cases
    c. The incidence rate is 10 per month

c. Neither incidence nor prevalence can be calculated from the information we have
d. None of the above

3. The annual incidence of diarrhoea in the school may be projected to be
a. 120 cases/1000/Year
b. 30 cases/1000/Year
c. 400 cases/1000/year
d. 10 cases/1000/year
e. None of the above

A first-year class of MPH students was 200. During the month of January, 2002 some students developed malaria fever. On 31st December 2002, 10 students reported to class with malaria fever but continued to attend class while on treatment and fully recovered by 5 January 2003. By 15 January 2003, twenty other students had also developed malaria and five of these had to miss class. During the entire period of January 2003, i.e. from 1st to 31st, forty different students had developed malaria and ten of these had missed classes.

4. The point prevalence of malaria on 1st January 2003 is:
a) 5% b) 50/10,000 c) 0.5% 0.05%

5. The point prevalence of malaria on 15th January 2003 is:
a) 5% b) 1% c) 10% 0.05%

6. The period prevalence rate of malaria 1st up to 15th January 2003 is:
a) 5% b) 15% c) 10% 0.05%

7. The cumulative incidence rate of malaria in January 2003 is:
a. 9 per 1000 per person day of observation
b. 7 per 1000 per person day of observation
c. 21%
d. 7% per person day of observation
e. None of the above

8. If 50 students started malaria prophylaxis on 11th January, and another 50 students started prophylaxis on 21st January, calculate the incidence rate of malaria for January (Assume that once prophylaxis is initiated, a student is no longer susceptible)
a. 9 per 1000 per person day of observation
b. 7 per 1000 per person day of observation
c. 9% per person day of observation
d. 7% per person day of observation
e. None of the above

9. In District X, there are 100,000 people. Previous studies have shown that TB incidence is 8 cases per 1,000 per year. If the average duration of TB is 21 months, the Prevalence Rate of TB per 1000 population can be estimated to be:
a. 160 cases
b. 14 cases
c. 800 cases
d. Prevalence cannot be calculated because time of interest is not stated
e. None of the above

10. Sensitivity and specificity are a measure of one of the following
a. Reliability
b. Correlation
c. Validity

d. All of the above
e. None of the above

11. Acceptable measures to describe the number of people who become sick after eating at the same restaurant on the same night are: Circle the most correct measure:

a. Period prevalence
b. Mortality index
c. Attack Rate
d. Point prevalence ratio
e. Crude death rate

12. The population at risk may refer to any of the following except:

a. A population which is susceptible to developing the disease of interest.
b. Part of a population which is susceptible to developing the disease of interest.
c. Its accurate measurement can be affected by selective undercounting of population groups in a census
d. The denominator used in calculating the maternal mortality rate

13. About standardisation:

a. In "direct" standardisation, we examine the Observed Rate and apply the stratum specific rates to a standard population to calculate the Expected rate. We the compute the Standardised Ratio
b. The SMR is the ratio of Expected deaths (Numerator) to Observed deaths (Denominator) and a Ratio greater that 1 suggests more mortality in than expected
c. In "In-direct" standardisation, we need to have the stratum specific rates of both comparison populations
b. In "direct" standardisation, we get strata specific rates and apply them to a specific standard population to compute adjusted rates

14. For many diagnostic or screening tests, there is a trade off between sensitivity and specificity. True statements include which one of the following?

a) Sensitivity would be extremely important when testing for Amyotrophic Lateral Sclerosis because there is no good treatment for it
b) Because hypothyroidism in infancy is devastating if missed, a screening test for it should be highly specific
c) Specificity is more important that sensitivity for screening tests
d) In evaluating the potential usefulness of a screening test, the effectiveness of treatment for the disease screened for is important

15. Residents of 3 villages, each one with a different water supply were asked to participate in a survey to identify cholera carriers. Since cholera deaths had occurred in the recent past almost every one participated. The proportion of residents that were carriers in each village was computed and compared. Classify the study:

a) Cross-sectional study
b) Case control study
c) Concurrent prospective cohort study
d) Experimental study
e) Non concurrent prospective cohort study

Use the following information for the next two questions: A doctor in the TB clinic examined 80 persons with prolonged cough and thought that 40 had tuberculosis. Laboratory examination of sputum showed that 30 of these patients had TB of whom 20 had been identified by the doctor's clinical examination.

16. The positive predictive value of the clinical examination is

a) 25%
b) 67%

c) 50%
d) Cannot be calculated
e) None of the above

17. The specificity of the clinical examination is
a) 60%
b) 75%
c) 50%
d) 25%
e) None of the above

2.3 Unit 3: ANALYTICAL EPIDEMIOLOGY

2.3.1 Introduction to the unit

Epidemiological inquiry often starts with observation of events, to detect abnormal trends, and to formulate hypotheses on possible explanatory factors for these trends. We can then conduct analytical investigations to test hypotheses, to test the strength of associations between factors and disease and to demonstrate a temporal relationship. The use of analytical techniques in the investigation of health events is what is termed as ***analytical epidemiology***. Cohorts and Case-control studies are the analytical techniques if interest in this unit. Other analytical techniques covered in subsequent units include interventional or experimental studies and comparative cross-sectional studies. The analytical process is a two-step process known as the ***epidemiological approach:***

Step1: We determine whether there is an association between a factor or characteristic (often called an exposure) and the development of a disease or other event of interest (often called an outcome). This can be done through studying characteristics of a group, characteristics of individuals or both

Step2: We derive appropriate inferences regarding a possible causal relationship from the pattern of associations that have been found

2.3.2 Unit Outline

In this unit, you will cover the following topics:

1. Cohort studies
2. Case – control
3. Assessment of risk
4. Analytical cross-sectional studies
5. Inferential Epidemiology: From Association to causation – deriving inference
6. Bias, confounding and interaction

2.3.3 Instructional Goal

This unit aims at equipping the student with the skills to: Design, conduct and analyse observational epidemiological studies that are descriptive and analytical in nature

2.3.4 Unit Objectives

By the end of this unit, the MPHO should be able to:

1. Design and conduct a cohort study
2. Design and conduct a case-control studies
3. Design and conduct a comparative cross-sectional study
4. Select appropriate study designs suited to a particular research question
5. Use Odds Ratios and Relative Risk to demonstrate the association between exposures and outcomes
6. Appraise the criteria used in causal inference

2.3.5 Time Frame

1 WEEK

2.3.6 Content

Session 1: Cohort Studies

Types of epidemiological study designs: The rule of twos

1. Observational studies
   a. Descriptive studies
      (i) Case-series/ecological studies
      (ii) Crossectional studies
   b. Analytical Studies
      (i) Cohort studies
      (ii) Case control studies
      (iii) Comparative cross-sectional studies
2. Experimental studies
   i. Clinical trials
   ii. Field Trials

In this Session, we shall delve into the design, conduct and analysis of one of the analytical study designs called the Cohort study.

Lesson Topics:

a. Design of a cohort study
b. Types of cohort studies
c. Potential biases in cohort studies
d. Advantages and disadvantages of Cohort study designs
e. *When to use a cohort study design*

Lesson Objectives:

The MPHO should be able to:

1. Set up a cohort study
2. To categorise study populations in terms of the exposed and the non-exposed
3. Distinguish the different types of cohort studies
4. Evaluate the potential biases in a cohort study design
5. Appraise the cohort study design to assess its advantages and disadvantages
6. Appraise different research problems to distinguish which ones warrant a cohort study design

a. Design of a cohort study

Introduction: This introduces you to one form of observational and analytical study design that is very often used to test hypotheses. It is used to test the relationship between risk factors or exposures and disease states. It has, therefore, unique features of design and outcome measures that are relied upon to draw inferences of causal relationships. These features distinguish it from other study designs, which you will also have to learn if you already have not done so.

What is a Cohort? You must have heard of the word cohort used in different contexts. Can you define in your own words what the word cohort means? Can you name at least groups of people that would ordinarily be referred to as cohorts? Write your definition(s) before you proceed.

In the strict sense of the term, a cohort is a group of people having or sharing the same experiences over time. In the epidemiological sense, it refers to a group of people who are usually subjected to a follow-up for whatever duration of time. In Epidemiology, cohorts are people who are defined by certain attributes like age, residence, occupation, etc. that are followed up in time and in whom a record of events e.g. disease or death is noted.

Why cohort studies? These are done usually because epidemiologists want to test hypotheses of "causal associations" between a given exposure/risk factor, and disease. Such hypotheses are usually derived from other less rigorous studies in analytical sense like case reports or case series, or cross-sectional studies that generate such hypotheses.

Design: A cohort study design is conducted as follows:
- Select a group of exposed individuals that are free of the outcome at baseline
- Select a group of non-exposed individuals that are also free of the outcome at baseline
- Follow up the groups to compare incidence of the outcome/events in exposed vs. non-exposed (the design may include two or more groups in each category)

Important features of cohort design

(1) At the beginning of the study, the persons to be studied have not yet developed the disease of interest.

(2) Both the exposed and unexposed individuals are at risk or capable of getting the outcome during the follow-up period.

(3) The exposure is known and can be measured in one way or another.

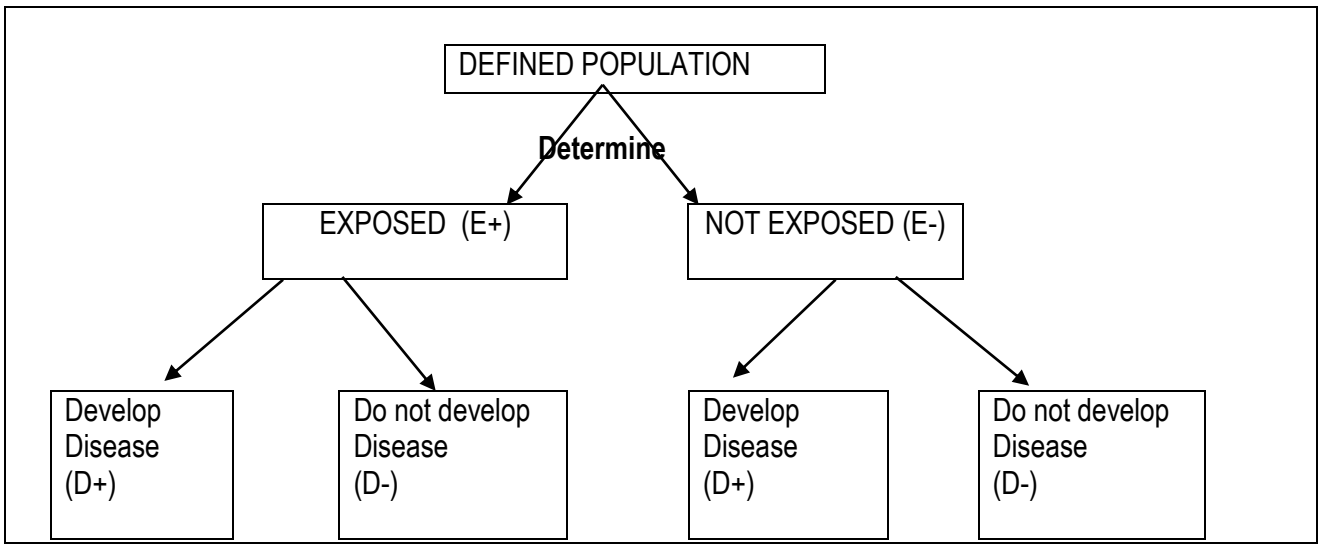
(4) Two groups of people from the same 'mother' population are followed up; one group has had or is under the exposure factor while the other group (the control group) is free of exposure factor. Both groups are followed up in time; both groups are initially disease free.

(5) During follow-up, incident cases of disease are noted and comparisons made through calculations of the risks or rates of developing the disease in both groups.

(6) By the very nature of this design, any suspected exposure factor precedes the onset of disease and therefore this type of design is quite useful in In showing the temporal relationship between an exposure and an outcome. Recall that temporality is a key criterion in Bradford & Hill's causal guidelines

(7) Cohort studies are observational and analytical in approach. The investigator will make/record observations on study subjects in the natural setting without any manipulation of factors in contrast to experimental studies. You may wish to peruse something about these as well. The investigator finally analyses the relationship of exposure factors and disease in the two groups, which are then compared.

Illustration



Analysis of outcomes: For a cohort study, we analyse the incidence of the outcome of interest in the exposed cohort and compare it to incidence of the outcome in the non-exposed cohort. *If a*

positive association exists between the exposed group and the exposure of interest, then the incidence in the exposed group is greater than the incidence in the non-exposed group. For two groups in which a binary outcome is expected, we can represent this information in a 2X2 table as follows:

Table: Analysis of Cohort Studies

		Exposure Status		
		Exposed	**Not Exposed**	
Outcome	**Disease develops**	a	b	(a+b)
	Disease does not develop	c	d	(c+d)
		(a+c)	(b+d)	(a+b+c+d)

Incidence in exposed = $\frac{a}{(a+c)}$

Incidence in non exposed = $\frac{b}{(b+d)}$

Example 2.3.1: Analysis of Cohort studies

	Exposure status		
Outcome	**Smokers**	**Non-smokers**	**Total**
Develop CHD	84	87	
Do not develop CHD	2916	4913	
Total	3000	5000	

Incidence in exposed (per 1000) = $\frac{a}{(a+c)}$ = 84/3000 x 1000 = 28/1000

Incidence in non exposed (per 1000) = $\frac{d}{(b+d)}$ = 87/5000x1000 = 17.4/1000

Selection of study populations: There are two ways; We mainly select study populations for inclusion in the study on the basis of whether they are exposed or not (e.g., currently smoking or not). We then follow up these two populations.

On the other hand, we can select a defined population before any of its members are exposed (e.g., on the basis of a factor related to the exposure e.g. a community neighbouring a new chemical plant) or before their exposures are identified (we take histories or laboratory measures to assess exposure). We then separate the population into those exposed and those not exposed.

b. Types of cohort studies

Broadly, there are three types of cohort studies:

1. ***Prospective cohort study*** (or concurrent prospective studies): In such studies, we select a population and characterise it on the basis of exposure at present or we follow them up till some get exposed. We then follow them on-wards to see whether they develop the disease or not. A major disadvantage of this design is the very long duration, the expense and possible loss to follow up of study subjects.

2. ***Retrospective cohort study*** (or historical cohorts): In such studies, we select a population of interest, and from the available records, see whether they were exposed several years ago (say 20 years ago). We divide them up on the basis of their status of exposure – say 20 years ago. We then track their record over the 20 years till the present time to see if they developed the disease or not. This design is shorter and less expensive. Its disadvantage is the lack of proper and complete records on each and every individual from the baseline record – say 20 years ago, and accurate periodic records over the 20 years.

3. ***Ambispective (or Ambi-directional) cohort study*:** A hybrid of the retrospective and prospective study designs. Here, we start with a record of initial exposure status, and trace for occurrence of the outcome till the present time. We then proceed to follow up the same cohort forward in time.

c. Potential biases in cohort studies

- Selection bias: Biases in assessing exposure statis leaning to misclassification of exposed people as non-exposed and non-exposed people as exposed
- Biases in assessing outcome: The person reading may be aware of the exposure status. We may reduce this by blinding.
- Information bias: This could be differential or non-differential, especially if the quality and depth of information obtained is different for exposed vs. non-exposed groups. We should minimise this by as much as possible trying to standardise the quality of information collected.
- Non-response bias: This may result from differential loss to follow up resulting in a selection bias
- Analytical bias: strong preconceptions in epidemiologist or statistician analysing the data

d. Advantages and disadvantages of Cohort study designs

Advantages/Strengths of Cohort study designs

(1) The suspected exposure factor levels are measured on each study subject at the beginning of the investigation and the disease has not yet developed. Therefore, there is a clearer temporal relationship between the exposure and the outcome. Cohorts are therefore very useful in measurements of time-relationships, relating exposure and time of onset of disease

(2) Because the exposure is measured before the occurrence of the outcome, disease status of subjects does not influence exposure measurement in the subjects; in other words differential misclassification of the exposure (information bias related to differences in the quality of the exposure assessment dependent on the outcome) is not a problem associated with this type of design.

(3) Cohort studies are most appropriate to study rare exposures e.g. the Hiroshima Atomic Bomb blast. These are rare exposures that do not occur under normal circumstances.

(4) They are useful to investigate multiple effects of an exposure or exposures, over time. One can test for example effect of smoking on the coronary vessels, as well as on the lungs over time, and can test the effects of smoking, H.T, Obesity on coronary heart diseases (CHD).

(5) Cohorts are very useful in measurements of time-relationships, relating exposure and time of onset of disease.

(6) With cohorts, it is easy to calculate the risk of developing disease through the use of incidence rates and risks.

Weaknesses/Disadvantages of cohort study designs

(1) It is almost practically impossible to investigate rare diseases using cohort designs because it would mean following up big numbers of subjects before a good number of cases would be realized on whom reasonable conclusions could be made.
(2) The nature of follow-ups makes the design quite expensive in a number of things: money, time, personnel, etc.
(3) Loss to follow-up of subjects is a very serious drawback in this design. This leads to bias if loss is not uniform in the two study groups.
(4) There is potential bias in assessing the outcome of exposure especially if such person doing the assessment knows the hypothesis under test, and which subject was exposed and not exposed.

e. When to use a cohort study design

When good evidence suggests an association between disease and an exposure, and when we are able to minimise loss to follow up, a cohort study is a good option. It is also better when the interval between exposures to development of disease is relatively short or when there is a good and complete recording system for important events (historical cohorts).

Lesson 2: Case-control Studies

Lesson Topics

a. Design of a case control study
b. Selection of cases and controls
c. Potential biases in case-control studies
d. Advantages and disadvantages of case-control designs

Lesson Objectives

By the end of this lesson, the MPHO should be able to:

1. Set up a case-control study
2. Select study groups in terms of the cases and the controls
3. Evaluate the potential biases in a cohort study design
4. Appraise the case-control study design to assess its advantages and disadvantages
5. Appraise different research problems to distinguish which ones warrant a Case-control study design

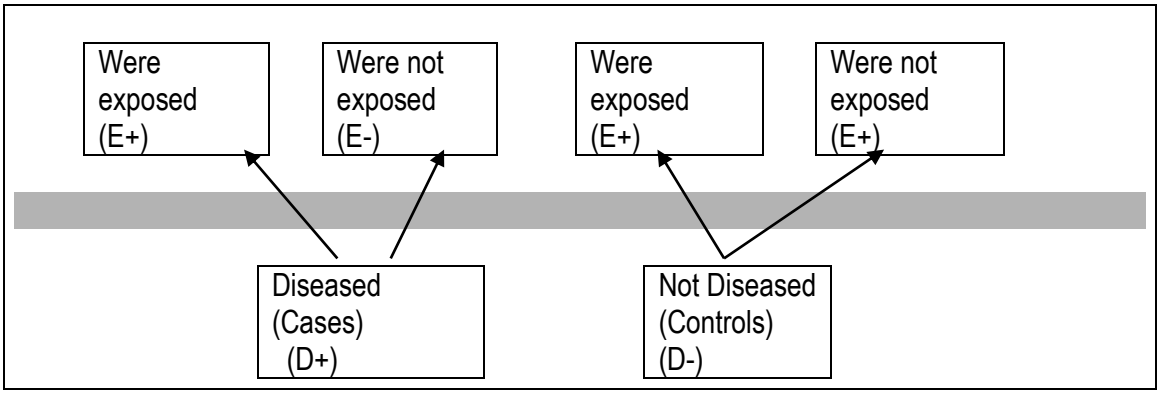
a. Design of a case-control study

Introduction: Case Control studies are "observational" studies. This means that the investigator does not actively determine who gets the exposure, but simply observes individuals or groups of individuals that already self-selected into the different exposure groups.

Conceptualizing case-control studies: In case control studies the relationship between cases of a particular disease with a possible exposure is investigated. In this study-design the investigator goes through the following steps:

- Identifying persons with the disease of interest i.e. the cases: the starting point is the people with the disease.
- Identify a comparable group of people without the disease who are the "control" group
- Establishing history of previous exposure to the suspected agent in both the cases and the controls
- Comparing frequency of exposure in the 2 groups

Illustration:



NB: Difference between a case-control study, a cohort and a crossectional study:
In a case-control study, the starting point is the people with disease. We then work backwards to assess whether they were exposed or not.

In a cohort, the starting point is the people who were exposed, then we follow then forward in time to see if they develop a disease or not.

In a crossectional study, we study both the suspected exposure and the disease at the same time (we cannot tell which preceded the other – ***the chicken or the egg?***

The time frame of case-control studies: The investigation process in case-control studies is retrospective. This is so because the process begins with identifying cases of a disease and then proceeds with inquiries about past exposure to the suspected causative agent. Similar inquiries are done for the controls and the two groups then get compared. Because the investigation looks back in time, it is called retrospective.

Nested case control studies: This is a hybrid design in which a case control study is nested in a cohort study. It reduces costs and duration of the study [Read about this study]

Analysis of case control studies: In the analysis of case-control studies we compare past exposure to the suspected agent between cases and controls. *We compare the proportion of cases that were exposed to the proportion of controls that were exposed.* If exposure is related to disease, we find that the proportion of cases that were exposed is greater than the proportion of controls that were exposed. It is important to note that because the cases and controls are the starting point, and not the population, there are two important arising issues:

1. It is not the rates of exposure that are compared; therefore, we cannot determine incidence/risk directly.
2. Rather, the odds of exposure to the suspected agent among cases are compared to the odds of exposure among the controls. The measure of association in case control studies is therefore called the *odds ratio* (It will be described later).

The findings of a case-control study can be represented in a 2X2 table as follows:

		First select		
		Cases	**Controls**	
Follow up past exposure	**Were exposed**	a	b	(a+b)
	Were not exposed	c	d	(c+d)
		(a+c)	(b+d)	(a+b+c+d)

We can then calculate the following:

Proportion of cases that were exposed = $\frac{a}{(a+c)}$

Proportion of controls that were exposed = $\frac{b}{(b+d)}$

How do we measure past exposure? It is through interviews, questionnaires, review of past medical and other records (e.g. employee records) and results of chemical/biological assays e.g. of blood and urine.

b. Selection of cases and controls

Selection of cases: Cases could be selected from hospitals, clinics, community/health centre registers or outreaches depending on the specific study question. Several problems arise out of this: If patients are selected from a single hospital, any risk factors identified may be unique to those patients because of the referral patterns of that hospital, and not the entire population. Criteria for eligibility must be written down in the protocol.

Incident vs. prevalent cases: Incident cases are newly diagnosed cases while prevalent cases are old cases. Incident cases may be disadvantageous because we have to wait for them. However, when we use prevalent cases, any risk factors observed may be related to survival with the disease and not actual development of disease. If more people who develop the disease die soon after, they will be under represented in a study that used prevalent cases. [Read further on this issue].

Selection of controls: It is one of the most difficult issues in epidemiology and it affects the internal validity as well as the generalizability (external validity) of this study. In most cases, the reference population is not defined. As such, the researcher must determine the source population that gave rise to the cases because this is the same population from which controls must be selected.

Sources of controls: Controls may be:

1. Non-hospitalized persons, in which we take a probability sample of the population, excluding those with the disease of concern. In practice, this is rarely possible
2. Non-hospitalized persons, in which we take information from registers e.g. Rosters, service lists or census records
3. Non-hospitalized persons, in which we get a control for each case, based on similarity of general background e.g. *neighborhood* controls or *best friend* controls
4. Hospitalized persons with a disease other than the one we are studying. However, the two diseases should not have related aetiology. Hospitalized controls are advantageous because it is more economical to select them, and they are more reachable. They are a captive population. However, the reference population for hospital controls is ill defined. It will be difficult to infer whether it is the cases or controls that actually differ from the general population. In addition, since we have to exclude controls with diseases of similar aetiology, we are at risk of having a control group in which the exclusion process results into a lower than expected prevalence of smoking than in the general population e.g. if we were studying the association of smoking and lung cancer, and excluded all people with emphysema, we may have a control group in which the prevalence of smoking is lower than that of the entire population, therefore affecting generalizability.

Activity 2.3.1 Recommended Reading
Problems in control selection**: Coffee vs. Cigarette smoking in the aetiology of lung cancer;** Gordis: Epidemiology; Pg. 146 to 147 (2nd Edition).

Marched case-control studies: In the marching of cases and controls, we select the controls in such a way that they are similar to the cases in certain characteristics that are not the concern of the study, but could distort the observed associations. There are two types of marching: frequency/group marching or individual marching. With group (frequency) marching, we select the controls such that the proportion of a given characteristic is similar with that in the cases. In individual marching, we select a control for each case, as similar as possible on the matched factor or factors. There are some problems with marching: If the characteristics to be marched are many, we may not find an appropriate control. In addition, if we march for a certain characteristic, then we cannot analyze its association with disease. We can also have unplanned marching, especially if we use best friends as controls. Marching that is in excess of what is planned is called over-

marching, and it may diminish the strength of the association between exposure and disease. In addition, matching in a case control study induces a selection bias that has to be adjusted for in the analysis.

Activity 2.3.2: Please read more about matching from the provided references.

Essential Reading

1. Epidemiology by Leon Gordis chapter 10
2. Designing Clinical Research by S.B. Hully
3. Basic Epidemiology by Beaglehole R, Bonita R and Kjellstrom. Published by W.H.O. 1993, Chapter 3.

Use of multiple controls: We can use multiple controls, either of the same type or different type. Multiple controls are advantageous because sometimes it is difficult to recruit cases and multiple controls of the same type can increase the power of the study. They are a multiple of the cases. Practically, a noticeable increase in power is seen up to the ratio of 1 case to 4 controls. Controls of different types improve on the generalizability of findings e.g. if we are concerned that hospital controls differ from the community.

c. Potential biases in case-control studies

Potential biases in case control studies include:

Problems with recall: Either limitations in recall (forgetting), recall bias (cases may be more keen to recall historical exposures more than controls) or reporting bias (deception).

d. Advantages and disadvantages of case-control designs

Case-control studies have got many advantages and their application in Public Health is increasing as more people become acquainted with them. The advantages include the following:

- They can be conducted quickly. This means that they can provide quick answers to explain current problems
- They are usually cheap compared to other types of studies
- Since there is no follow up period, study subjects cannot be lost
- They are suited to investigating rare conditions

Case control studies are, however, susceptible to many types of bias, which can lead to wrong conclusions if they are not planned carefully and conducted rigorously. While planning a case control study the following issues need to be carefully scrutinized in order to minimize bias.

- Selection of cases
- Selection of controls
- Recall problems
- Interviewer bias

You will need to read more about case-control studies in the reading materials and textbooks so as to fully appreciate the influence of each of these issues on the case-control study design.

Lesson 3: Assessment of Risk

Introduction: The immediate outcome measures in analytical studies are proportions of the outcome in each study group. In cohorts, the incidence of disease in the exposed is compared with that in the non-exposed. In case-control studies, the proportion that was exposed in the cases is compared with the proportion that was exposed in the controls. Regardless of which design is used, the objective is to determine whether there is excess risk associated with a particular exposure. How do we determine that the risk on one group is higher than the risk in another group? There are some measures used to compare risk between different populations. These will be the subject of this lesson.

Lesson Topics:

a. *The Absolute Risk*
b. The Relative Risk
c. The Odds Ratio
d. The Attributable Risk: Estimating the potential for prevention

Lesson Objectives:

By the end of this lesson, the student should be able to:

1. Distinguish between the absolute risk and the relative risk
2. Apply the relative risk in the measurement of the strength of the association between factors and events
3. Appraise the use of Odds ratios in measurement of association between factors and disease
4. Synthesize scenarios in which the attributable risk is useful in estimating the potential effect of prevention interventions

a. The absolute risk

The incidence of a disease in an exposed population denotes the probability of one getting the condition. It is non-comparative and is known as the absolute risk. It may also be simply referred to as a risk or an incidence.

b. The Relative Risk and Risk Difference

There are two possible ways of comparing risk to determine excess risk: We can use the ratio of the incidence in exposed to incidence in non-exposed (relative risk) or we can subtract one from the other (risk difference).

Example 2.3.2: Relative risk as a proportion or a difference

Food	**A** **Ate (% sick)**	**B** **Did not eat (% sick)**	**C** **(A)/(B)**	**D** **(A)- (B)**
Egg salad	83	30	2.77	53
Macaroni	76	67	1.13	9
Cottage cheese	71	69	1.03	2
Tuna salad	78	50	1.56	28
Ice cream	78	64	1.21	14
Other	72	50	1.44	22

However, does the method we choose to calculate excess risk make any difference? Consider the table below:

	Population	
	A	**B**
Incidence		
In exposed	40	90
In non-exposed	10	60
Difference in incidence rates	30	30
Ratio of incidence rates	4.0	1.5

We note here that while the difference in incidence rates is the same, the ratio of incidence rates shows a greater association in one community than another. The relative risk (RR) or risk ratio is defined as the ratio of the incidence of disease in exposed to the incidence of disease in the non-exposed:

$$RR = \frac{\text{Incidence of an event among exposed people}}{\text{Incidence of an event among unexposed people}}$$

		Exposure Status		
Outcome		**Exposed**	**Not Exposed**	
	Disease develops	a	b	(a+b)
	Disease does not develop	C	d	(c+d)
		(a+b)	(b+d)	(a+b+c+d)

Incidence in exposed = $\frac{a}{(a+c)}$ **Incidence in non exposed =** $\frac{b}{(b+d)}$

Therefore, the Relative risk = $\frac{a/(a+c)}{b/(b+d)}$

Example 2.3.3: Calculation of relative risk

	Exposure status		
Outcome	**Smokers**	**Non-smokers**	**Total**
Develop CHD	84	87	
Do not develop CHD	2916	4913	
Total	3000	5000	

Incidence in exposed (per 1000) = $\frac{a}{(a+c)}$ = 84/3000 x 1000 = 28/1000

Incidence in non exposed (per 1000) = $\frac{d}{(b+d)}$ = 87/5000x1000 = 17.4/1000

Therefore, the Relative Risk = 28/17.4 = **1.6**

Interpreting the value:
If the RR = 1: Then risk in exposed = Risk in non-exposed therefore no association
If the RR > 1: Then risk in exposed > Risk in non-exposed therefore a positive association
If the RR < 1: Then risk in exposed < Risk in non-exposed therefore a negative association

Application of the Relative Risk: In cohort studies, it is possible to derive incidences directly in the exposed and non-exposed groups. The relative risk is therefore used in the analysis of cohort studies.

c. The Rate Ratio and Rate Difference: Similar to risks, there are two possible ways of comparing rates to determine excess rates: We can use the ratio of the incidence rates in exposed to incidence in non-exposed (rate ratio) or we can subtract one from the other (rate difference).

$$\text{Rate} = \frac{\text{Number of new cases}}{\text{Total person time of observation}}$$

$$\text{Rate Ratio} = \frac{\text{Rate in the exposed}}{\text{Rate in the unexposed}}$$

Rate Difference= Rate in the exposed-Rate in the unexposed

Example 2.3.4 Calculation of the rate ratio and rate difference

	Exposed	Unexposed
New cases	30	10
Total person years of observation	1000	1100

$$\text{Rate Ratio} = \frac{\text{Rate in the exposed}}{\text{Rate in the unexposed}}$$

$$\text{Rate Ratio} = \frac{30/1000}{10/1100}$$

Rate Ratio= 3.3
Rate Difference= 30/1000-10/1100=0.02/person year of observation or 2/person year of observation

d. The Odds Ratio
Background: In case-control studies, we cannot determine incidence from the available information on study groups, and therefore, we cannot compute the relative risk directly. We use another measure of association – the Odds Ratio.
Definition: It is defined as the ratio of the odds of exposure among the cases divided by the odds of exposure among the controls.

$$\text{Odds ratio} = \frac{\text{Odds of exposure in the cases}}{\text{Odds of exposure in the controls}}$$

The important question is:
How are the odds computed?

Odds: The ratio of the number of ways in which an event can occur

$$\frac{\text{Chances that an event will occur}}{\text{Chances that an event will not occur}}$$

$$\frac{\text{Chances that a horse will win the race: P (60\%)}}{\text{Chances that a horse will not win the race: (1-P) (40\%)}} = 1.5$$

The Odds ratio in case-control studies: The following table summarizes findings related to exposure among a group of cases and a group of controls.

		First select		
		Cases	**Controls**	
Follow up past exposure	**Were exposed**	a	b	(a+b)
	Were not exposed	c	d	(c+d)
		(a+c)	(b+d)	(a+b+c+d)

From this table:

The odds of exposure among the cases

$$\frac{\text{Probability that a person who has disease was exposed } a/(a+c)}{\text{Probability that a person who has disease was not exposed } c/(a+c)} = \frac{a}{c}$$

The odds of exposure among the controls

$$\frac{\text{Probability that a person who has no disease was exposed } b/(b+d)}{\text{Probability that a person who has no disease was not exposed } d/(b+d)} = \frac{b}{c}$$

Therefore odds ratio = a/b divided by c/d $= \frac{\mathbf{a\,d}}{\mathbf{b\,c}}$

Interpreting the Odds Ratio: The Odds ratio is interpreted in a similar way to the Relative Risk
If the OR = 1: Then risk in exposed = Odds in non-exposed therefore no association
If the OR > 1: Then risk in exposed > Odds in non-exposed therefore a positive association
If the OR < 1: Then risk in exposed < Odds in non-exposed therefore a negative association

Situations in which the Odds ratio is a good estimate of the Relative Risk: Situations in which the calculated odds ratio approximates to the relative risk are:

1. When the cases are representative of all people with the disease in the population and the controls are representative of all people without the disease
2. When the disease being studied does not occur frequently, i.e., when the disease is rare
3. When controls are sampled using the case-based sampling technique (Read about sampling techniques)

Exercise 2.3.1: Analysis of case-control studies

An outbreak of diarrhoea occurs in a student's hostel. You go to investigate this outbreak and some of the suspect foods include the pancakes that students buy from hawkers to accompany their morning tea. In your investigation you find that 50 students from the hostel reported diarrhoea episodes in the past 24 hours while 60 students from the same hostel did not.

Study questions

1. How many cases were identified?
2. How many controls were identified?

Further inquiry reveals that among the cases, 40 had eaten cassava pancakes with their tea. Among the students without diarrhoea, however, it was found that 15 had eaten cassava pancakes with their morning tea.

Study questions

1. Draw a table to show the findings
2. What are the odds of exposure in the cases?
3. What are the odds of exposure among the controls?
4. Calculate the odds ratio

Solutions to study problems

1. Number of cases = 50
2. Number of controls = 60

Table 2.1 showing those who ate pancakes among cases and controls

	Ate pancakes	Did not eat	Total
Cases	40	10	50
Controls	15	45	60
Total	55	55	110

4. Odds of exposure among the cases = 40/10
5. Odds of exposure among controls = 15/45
6. Odds ratio = $\frac{40 \times 45}{10 \times 15} = 12$

d. The Attributable Risk: Estimating the potential for prevention

The attributable risk (also called the attributable risk proportion) answers the question: How much of the disease that occurs can be attributed to a certain exposure? This is the critical issue for policy-makers is what proportion of the disease incidence will be averted if the exposure is controlled. The attributable risk can be defined as the proportion of disease risk or incidence that can be attributed to a certain exposure. It is the incidence rate (or death rate) of disease among exposed persons minus incidence rate (death rate) of disease among unexposed. Attributable risk may be further developed into another measurement as shown below:

The attributable risk percent or fraction =

$$\frac{\text{(Incidence in exposed) – (Incidence in non- exposed)}}{} \times 100$$

(Incidence in exposed)

Another related measure is known as Population Attributable Risk (PAR). This is an estimate of excess ate of disease in the total study population (i.e. both the exposed and unexposed) that we could ascribe to the reason of exposure.

The Population Attributable Risk (PAR) =

$$\frac{\text{(Incidence in total population) – (Incidence in non- exposed)}}{\text{(Incidence in total population)}} \times 100$$

Illustration: Comparing Relative Risk and Attributable Risk

(a) Relative Risk

Lung cancer:	Mortality risk – Smokers:	140
	Mortality risk – Non-smokers:	10
	Therefore, RR = 140/14 =	14
CHD:	Mortality risk – Smokers:	669
	Mortality risk – Non-smokers:	413
	Therefore, RR = 669/413 =	1.6

Observation: The relative risk is much higher for smoking and lung cancer than for CHD.

(b) Attributable Risk

Attributable Risk in lung cancer: $\frac{140 - 10}{130}$ = 92.9%

Attributable risk in CHD: $\frac{669 - 413}{669}$ = 38.3%

Exercise 2.3.2

In a population of 1000 people, 400 are alcoholics and out of these alcoholics 150, developed liver cirrhosis, the rest of the population were teetotallers and out of these only 40 developed liver cirrhosis.

(1) Summarize this information in a tabular form.
(2) Calculate the relative risk for development of liver cirrhosis.
(3) Calculate attributable risk and attributable risk percent.
(4) In your opinion, is a relative risk a rate or a ratio? Give your reasons.
(5) What do you think are basic differences between Relative risk and attributable risk?
(6) Calculate the population attributable risk.

Important steps/issues to consider in Exercise 2.3.2

(1) Generate a 2 by 2 table relating exposure factor (alcohol consumption/non alcoholic consumption) against outcome of interest (liver cirrhosis).
(2) Calculate incidence rates among the exposed (alcoholics and the unexposed (teetotallers).
(3) Calculate RR using findings in (2) above.
(4) Calculate Attributable Risk using (2) above.
(5) Calculate Attributable Risk percent using (4) and (2).

(6) Using information in (3) and (4) above, Population Attributable Risk should be completed.

Note the following: Attributable Risk is the difference between rates of disease in the exposed and unexposed, while Relative Risk simply indicates the ratio of the rates of disease in the exposed to the unexposed population. The AR therefore, attempts to quantify absolute effect of exposure above the baseline level; it indicates what the excess risk is among the exposed over and above the unexposed. The RR on the other hand is a measure of strength of association between exposure and disease. Thus, a RR of 2 or 3 or 4 etc. would be referred to as a twofold, threefold etc. difference. Therefore RR provides some evidence that can be used to arrive at an inference of causal relationship.

References

(1) Epidemiology by Leon Gordis
(2) Basic Epidemiology by Beaglehole
(3) Epidemiology in Medicine by Charles Heinekens
(4) Foundations of Epidemiology by Abraham Lilienfeld

Session 4: Analytical Crossectional Studies

Introduction: Although there are mainly designed to be descriptive, cross-sectional studies can also be used to compare outcomes in groups with different exposures. Although we may not have sufficient evidence to infer causality, we are able to test for associations between exposure and disease. In this session, we build on the previous discussion of crossectional studies to discuss comparisons in crossectional studies.

Session topics

a. *Comparing sub-groups in a single sample cross-sectional study*
b. *Crossectional comparative studies*
c. *Analysis of cross-sectional studies involving comparison*

Session objectives: By the end of this session, the student should be able to:

Design a cross-sectional study that allows comparison of outcomes between different presumed exposure groups Analyze the outcomes of cross-sectional study that involves comparison

a. Comparison in crossectional studies

Although crossectional studies are mainly meant to be descriptive and to generate prevalence data, it is quite common to conduct comparisons to test association between presumed 'exposure factors' and particular health related outcomes.

There are two ways that we can set up crossectional studies to allow for comparisons:

1. We may compare population sub-groups in a single sample study if the sample is sufficiently large or the prevalence allows sufficient numbers in comparison sub-groups. In such cases, we select one sample and determine the distribution of the characteristics of interest. The variable that represents the outcome of interest is then used to divide the population into two groups – those who have the outcome of interest and those who do not. Thereafter, we compare exposures in the two groups. It should be noted here that using this approach, we often obtain unequal comparison groups because in most cases the prevalence of key population characteristics is such that the majority of the people have a certain status and while the minority has the alternate status.

Example: Take for example a study conducted to determine the prevalence and factors associated with hypertension. We take a single sample (assume it is 1000 individuals). Assume that we find that the prevalence of hypertension is 24% i.e. 240 people have hypertension while 760 do not. In this case, the 240 people with hypertension can become the 'people with the outcome' while the 760 are the 'people without the outcome of interest'.

We can then compare the two groups to determine the proportion of the 240 people with hypertension who are overweight (the presumed exposure) and the proportion of the 760 people without hypertension who are overweight.

Assume that we find that among the 240 people found to have hypertension, 25% (i.e. one quarter or 60 people) are overweight while among the people without hypertension, 10% (i.e. one tenth or 76 people) are overweight. These findings can be represented in a 2X 2 table as follows:

Illustration:

		'Presumed Outcome Status'		
		With hypertension	**Without Hypertension**	**Total**
'Presumed Exposure Status'	**Overweight**	60	76	136
	Not overweight	180	684	864
	Total	240	760	1000

We then compute the measures of association. The difference with this type of approach in that the sizes of the outcome groups depend on the prevalence of the outcome in the population of interest. In order for this to work therefore, we ought to have a sample size that is large enough to allow sufficient numbers of 'people with hypertension' for us to be able to make comparisons regarding overweight.

2. We may set up a study in which we select a pre-determined number of people with hypertension (say 500) and a predetermined number without hypertension (say 500). We then compare the prevalence of obesity in either groups. This design looks exactly like a 'case-control' study, the only difference being that both the presumed outcome and presumed exposure are assessed at the same time meaning that there is no temporal relationship.

b. Analysis of crossectional comparative studies

Comparisons in crossectional studies can be conducted in the same way we analyze cohorts (We determine the Prevalence Ratios. On the other hand, they can also be conducted in the same way we analyze case control studies (We determine the Odds Ratios). The findings can be represented in a 2X2 table as follows:

Illustration:

		'Presumed Outcome Status'		
		Disease	**No Disease**	
'Presumed Exposure Status'	**Exposed**	a	b	(a+b)
	Not exposed	c	d	(c+d)
		(a+c)	(b+d)	

- We can determine the prevalence of disease in persons with a manifest exposure **(a/(a+b))** and compare with the prevalence of disease in persons without manifest exposure **(c/(c+d)), following which we determine the Prevalence Ratio**
- **OR**
- We can determine the prevalence of manifest exposure in persons with a disease **(a/(a+c))** and compare with the prevalence of manifest exposure in persons without the disease **(b/(b+d)). However, in this case, we cannot compare the proportions directly but we compute the odds ratios [a/(a+c)/c/(a+c)] ÷ [b/(b+d)/d/(b+d)], following which we determine the Odds Ratio**

Exercise: Using the data from the example on hypertension (in the table below):

		'Presumed Outcome Status'		
		With hypertension	**Without Hypertension**	**Total**
'Presumed Exposure Status'	**Overweight**	60	76	136
	Not overweight	180	684	864
	Total	240	760	1000

a) Compute the Prevalence Ratio
b) Compute the Odds Ratio
c) Comment on the difference between the two. Based on what you know, in what circumstances would these two estimates be nearly equal?

Lesson 6: Inferential Epidemiology: From Association to Causality – Deriving Causal Inference

Introduction: The epidemiological approach is a two-step inquiry about the aetiology of disease or promotion of health-related states. It is a two-step approach:

Step 1: Determine association between plausible factors and health related events by studying characteristics of the events

In groups – ecological studies: in ecological studies, we do not have data on individuals, but information on groups. There is a problem on inference here, described as the ecological fallacy

In individuals – case-control studies or cohorts: These are more analytical studies in which we have information on individuals

Step 2: Determine the causal relationship: If there is an association, is it really causal?

When we find an association in epidemiology, we do not conclude straight away that it is causal. The association could have been caused by confounding or bias. In this lesson, we shall highlight some important issues to consider in inferring causality.

Lesson Topics:

a. *Types of association*
b. Evidence of causation
c. An introduction to bias in epidemiological studies
d. An introduction to confounding and interaction

Lesson Objectives:

By the end of this session, the MPHO should be able to:

1. Appropriately appraise disease causal pathways to distinguish the different types of causal relations
2. Apply Hill's criteria in inferring causality

a. Types of association

Real/Spurious associations: The purpose of epidemiological inquiry is to enable us to examine associations to draw conclusions on causality. Associations may be *real* or *spurious* (due to confounding or interaction).

The causal pathway: The causal pathway may be direct or indirect. In the direct pathway, a factor directly causes disease while in the indirect pathway, there are intermediate steps involved. In humans, intermediate steps are almost always present in any causal process.

Types of causal relations: If the relationship is causal, there are 4 possible types of relations:

(i) *Necessary and sufficient:* Without a factor, there is no disease. When the factor is present, there is always disease.

(ii) *Necessary but not sufficient:* The factor is necessary and must be present for disease to occur. However, it is itself not sufficient and multiple factors are involved, often in a temporal sequence.

(iii) *Sufficient but not necessary:* A factor alone can produce the disease, but so can other factors.

(iv) *Neither sufficient nor necessary:* A factor is neither enough to cause a disease (multiple other factors are needed) nor is it necessary because other factors can cause the disease. This is the commonest situation in real life.

b. Evidence of causal relation

Koch's postulates: This is an example of the process of evolution of criteria for causal inference. Koch in the 19th century, while studying the aetiology of Tuberculosis, postulated that in order for one to conclude that an organism causes a particular disease;

1. The organism must always be found with that disease
2. The organism is not found in any other disease
3. The organism, when isolated from a person with a disease, cultured through several generations and inoculated in experimental animals will produce the disease.

These postulates were not accurate but were an important start. In this century, however, there is an increasing emergence of diseases that are not caused by organisms.

Guidelines for judging whether an association is causal: The following guidelines, also known as *Hill's criteria*, are important considerations in inferring causality:

1. Temporal relationship
2. Strength of the association
3. Replication of findings
4. Biological plausibility
5. Dose-response relationship
6. Consideration of alternative explanations
7. Cessation of exposure
8. Specificity of the association
9. Consistency with other knowledge

Activity 2.3.3: Please read more and expound on Hills criteria for causal inference. Identify the 4 most important criteria. [NB: These concepts will be developed further in the course: Applied Epidemiology II]

c. Introduction to bias in epidemiological studies

Definition of bias: Any systematic error in the design, conduct or analysis of a study that results in a mistaken estimate of an exposures effect on the risk of disease. Bias can occur at the design stage, data collection stage, and data handling stage.

1. Bias in Design: This includes selection biases that could be further classified as inclusion or exclusion biases.

2. Bias in Data collection: Information bias that includes recall bias, recall limitation and misclassification bias. In misclassification bias, there is a misclassification in a study group e.g., a person with no disease is classified as having a disease or vice versa. In differential misclassification, the error is more in one group than another (e.g. more in the cases than the controls). It is a more severe form than non-differential misclassification in which the error is the same either way. Non-differential misclassification however tends to diminish the strength of the observed association. Other biases in data collection include:

(1) *Surveillance bias:* Disease may be better monitored in an exposed population than in an unexposed population, especially in cohort studies.

(2) *Reporting bias:* Intentional refusal to give certain information. "Wish bias" is an example of this: a smoker developing lung cancer may deny having smoked a packet a day, and instead report that they smoked only 2 cigarettes a day.

(3) *Failure to account for confounding:* If we fail to recognize and plan for confounding

3. Bias in data handling: These include analytical bias, in which the investigator may bias their analysis – The investigator is the police, prosecutor and the judge.

Avoiding biases: The best way to avoid bias is to anticipate it and put in place measures to avoid it in the design, conduct and analysis stages. Other more robust approaches include *blinding* or *masking*, that are mainly employed in experimental studies. Please refer to the earlier lessons on cohorts and case-controls to further characterize the biases that are commoner in particular study designs.

d. Introduction to confounding and interaction in epidemiological studies

A problem in epidemiological studies is that if we observe an association – is it a true association or in fact is due to confounding by a third factor. In this topic, we introduce confounding. [However, the topic will be covered in detail in Applied Epidemiology II]

1. Confounding

Confounding is one of the most important challenges in observational epidemiological studies, especially in causal inference. The observed relationship may not be causal, but may be due to another factor that is causal and is related to the factor we are making inference on so that the apparent association is in fact due to the third factor and not the factor we suspect.

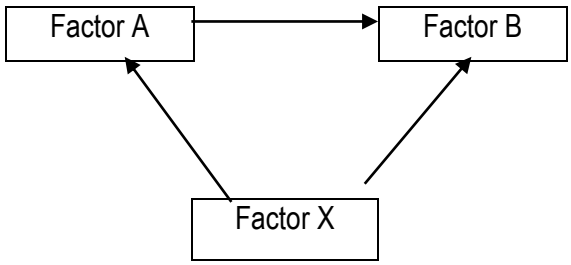
Illustration: In a study of whether factor A is a cause of factor B, we say that a third factor X is a confounder if the following are true:

1. That X is a known risk factor for disease B
2. That X is associated with factor A, but is not a result of factor A

Example: We find that coffee drinking (factor A) is related to lung cancer (factor B); this could mean that coffee actually causes cancer. It could also actually mean that people who smoke tend to take coffee than those who do not smoke. Smoking in this case is a confounder (factor X) because it is a known risk factor for lung cancer, it is associated with coffee consumption, but is not a result of coffee consumption i.e. we observe the association of coffee drinking and pancreatic cancer simply because cigarette smoking causes lung cancer and most smokers take coffee.

Deduction: When we observe an association, we should ask whether it is actually causal, or is due to a third factor that is both a known risk factor for a disease, and is related to the factor we are interested in.

The causal pathway showing confounding



Factor X is associated with factor B; however, it is also related to factor A, but is not necessarily caused by it. It is also not part of the direct causal pathway between factor A and B i.e. it is not an intermediary factor

Approaches to confounding: Confounding can be controlled for at the design stage or at the data analysis stage. At the design stage we can do individual or group marching while at the analysis stage, we can employ stratification or statistical modeling (adjusted analysis). [These techniques will be covered in detail in Applied Epidemiology II].

2. Interaction

When the incidence rate or association with two or more risk factors differs from the sum total of their individual effects, then we conclude that there is an interaction between these factors in leading to the event in question. It means that the two factors actually enhance or diminish each other to create an effect that is higher than expected even if their individual effects were added up. We therefore talk of positive interaction (synergism) or negative interaction (antagonism). [These techniques will be covered in detail in Applied Epidemiology II].

To detect confounding us:

3. Determine association
4. If there is association, we eliminate confounding
5. We then calculate the individual strengths of association, and the pooled strengths; if the pooled strength of the association is more or less that a combination of the individual strengths, we report that there is interaction.

2.3.7 Extension Activities

Extension Activity 1: Discussion Forum Question
Analytical Epidemiology includes Cohort studies, Case-control studies, Assessment of Risk as well as causal inference. For this forum, we shall focus on analytical study designs. What key features distinguish the Case-Control Studies from Cohort studies their advantages and disadvantages

Extension Activity 2: Self- Assessment Quiz

QUIZ 2.3.1 *(Choose one correct option)*

Use the following information to answer questions 1 – 6. Dr. Kisitu is the DDHS of Wakiso District. An outbreak of Cholera occurred in Wakiso District in the month of November 2004. Dr Kisitu found that 15 of the 20 households with cases did not have a latrine, while 22 of the 30 controls in the study had a latrine in the home.

1. What type of study design did Dr. Kisitu employ?
    a) Cohort
    b) Crossectional
    c) Case control
    d) Clinical Trial
    e) None of the above

2. What are the Odds that a case had a latrine at home?
    a) 5/15
    b) 15/20
    c) 5/20
    d) 15/5

3. What are the Odds that a control had a latrine at home?
    a) 22/30
    b) 6/20

c) 22/8
d) 8/30

4. What is the Odds Ratio for the association between cholera and absence of a latrine?
a) 0.12
b) 1.5
c) 8.25
d. 0.67

5. Is the absence of a latrine, the cause of Cholera?
a) Yes
b) No

6. If 6 of the 20 cases died, what is the case fatality rate?
a) 60%
b) 42.9%
c) 30%
d) 100%

7. Which of the following is a case control study?
a) A study of the past mortality or morbidity trends to permit estimates of the occurrence of disease in the future
b) Analysis of previous research in the different places and under different circumstances to permit establishment of hypotheses based on the cumulative knowledge of all known factors
c) Obtaining histories and other information from a group of known cases and a comparison group to determine the relative frequency of a characteristic or exposure under study
d) Study of the incidence of cancer in men who have quit smoking
e) Both “a” and “c”

8. In a study begun in 1965, a group of 3000 adults in Baltimore were asked about alcohol consumption. The occurrence of cases of cancer was studied in this group between 1981 and 1995. This is an example of a:
a) Cross-sectional study
b) Concurrent cohort study
c) Retrospective cohort study
d) Clinical trial
e) Case-control study

9. In a case-control study, which of the following is (are) true. Select the non-true option
a) The proportion of cases with the exposure is compared with the proportion of controls with the exposure
b) Disease rates are compared for the people with the factor of interest and for people without the factor of interest
c) The investigator may choose to have multiple comparison groups
d) Recall bias is a potential problem

10. Control of confounding can be addressed at the following stages of research
a) During data collection
b) Through the definition of eligibility
c) During the interpretation of data
d) Only a, b and c

11. The following problems are associated with the following:
a) Cross-sectional study design is not suitable for investigating a disease with a long latent period
b) One cannot measure directly the incident rate in ecological study designs
c) Study of multiple effects of an exposure is done using a cohort study design

d) Only A and B are the problems

12. In a case-control study of ovarian cancer, there were 235 cases and 451 controls. 40 cases and 118 controls reported that they had used oral contraceptives. The estimated risk (Odds Ratio) of ovarian cancer associated with the use of contraceptives is:

a) 0.58
b) 0.65
c) 1.73
d) 1.54
e) 0.69

13. All of the following statements describe the advantages of a cohort study over a case control study when assessing possible risk factors for disease except:

a) Prospective data collection used
b) There is less chance for bias in data collection or subject recall
c) A cohort study is more likely to explain causation
d) True incidence rates for disease can be determined
e) None of the above

14. In a marched case control study, the following results were obtained:

Controls		Cases	
		Exposed	Not exposed
	Exposed	A	B
	Not exposed	C	D

The Odds Ratio is

a) ad/bc
b) a/d
c) c/b
d d/a

Questions 15 and 16 are based on the following statement:
Factor A, B and C each individually cause a certain disease without the other factors, but only when followed by exposure to factor X. Exposure to factor X alone is not followed by diseases, but the disease never occurs in the absence of exposure to factor X.

15. Factor X is:

a) A necessary and sufficient cause
b) A necessary but not sufficient cause
c) A sufficient but not necessary cause
d) Neither necessary nor sufficient

16. Factor A is:

a) A necessary and sufficient cause
b) A necessary but not sufficient cause
c) A sufficient but not necessary cause
d) Neither necessary nor sufficient
e) None of the above

2.4 Unit 4: INTERVENTIONAL EPIDEMIOLOGY

2.4.1 Introduction to the Unit

We would like you to appreciate that ***observational*** studies are those studies in epidemiology that do not involve any intervention or experiment. In such studies nature is allowed to take its course, with changes in one characteristic being studied in relation to changes in another characteristic(s). The investigator merely observes events in nature without intervention or manipulation other than to record, classify, count and analyse the observations or data. This process of merely observing events as they occur in nature and analysing the observations constitutes the field of observational epidemiology.

Experimental studies on the other hand are those, which involve an experiment or an intervention. An experiment is defined as a study in which the investigator intentionally alters one or more factors under controlled conditions in order to study the effects of doing so. In experimental studies, therefore, the investigator has direct control of the conditions under which the study is conducted such as allocation of study individuals to experimental group or control group. It is common to refer to these studies as trials. These studies or trials fall within the field of experimental or interventional epidemiology. It therefore follows that observational study designs should be used when studying harmful exposures while experimental or interventional study designs should be used when studying possibly beneficial exposures such as a drug or vaccine. In a study of the effect of cigarette smoking and lung cancer it would be unethical to allocate some individuals to smoke 1 pack of cigarettes per day while others smoked none but perfectly ethical for one to merely observe individuals who have selected to smoke through some natural factors not under the control of the investigator.

Recap of Types of Epidemiological Studies

i) Observational Studies
- A. Descriptive Studies
  - Case reports/studies/series and Ecological studies
  - Cross-sectional studies
- B. Analytical Studies
  - Case-Control Studies (retrospective)
  - Cohort Studies (prospective/longitudinal)
  - Comparative Cross-sectional studies

ii) Experimental Studies
- A. Clinical Trials (RCTs)
- B. Community Trials

2.4.2 Unit outline

The following topics will be covered:

1. Introduction to Interventional Epidemiology
2. Clinical Trials
3. Community Trials
4. Analysis if experimental studies
5. Ethics in Research

2.4.3 Instructional Goal

This unit will enable the student with the skills to discuss the principle concepts of epidemiological interventions, and how they can be applied to disease prevention and control

2.4.4 Unit Objectives

By the end of this unit, the student should be able to:

1. Describe key concepts in interventional epidemiology
2. Design, conduct and interpret the findings of clinical trials
3. Design conduct and interpret the findings of community trials
4. Evaluate the key ethical considerations in interventional studies

2.4.5 Time Frame

1 WEEK

2.4.6 Content

Lesson 1: Introduction to Interventional Epidemiology

Lesson Outline

a. *History of Interventional/Experimental Epidemiology*
b. Comparing cohorts with randomised trials
c. Objectives of intervention trials
d. Types of intervention trials

Lesson Objectives:

The objective of this session is to equip the MPHO with the skills to be able to explain the basic principles underlying the rationale of interventional studies

a. History of Interventional/Experimental Epidemiology

Petrarch and Lind: In 1334 Petrarch introduced the concept of comparison in empirical studies of interventions and also introduced the clinical trial. Another important personality in the history of interventional epidemiology was Lind. **James Lind** was a physician in the early 18th century, when scurvy was a major problem among sailors on long sea voyages. At that time, the cause of scurvy was not known. Bad air, congenital laziness and indigestible food were all suggested as possible causes. Lind observed that the sailors' diet was very poor, consisting of biscuits and salted fish or meat. The diet was deficient in fruits and vegetables. In 1747 he conducted an experiment at sea with a population of 12 patients suffering from scurvy. In this experiment, Lind divided his population into groups and allocated different interventions to each group. The interventions consisted of different types of food supplements including lemons and oranges in one group. He then followed these patients to record whether there was any clinical improvement of the scurvy. He observed, "….the most sudden and visible good effects were perceived from the use of oranges and lemons …. "

Lind's experiment is thus an early example of a controlled experiment or an interventional study. He had a potentially beneficial exposure, he controlled who got what intervention and observed his

patients for a beneficial outcome. What was particularly important was that he had comparison or "control" groups of patients who did not receive the intervention of interest, which meant that he could compare the outcome in those who received the intervention to those who did not.

The first classic randomised controlled trials were used in the 1950s. An early example was in the investigation of the efficacy of streptomycin in the treatment of tuberculosis. Since then, this method has been increasingly used to evaluate new treatments and interventions.

ACTIVITY 2.4.1

Using the internet find the following information:

1. Who was Petrarch and what led him to discuss the concept of comparison groups?
2. Briefly describe the design of the efficacy trial of streptomycin in the treatment of tuberculosis conducted in the 1950s.

b. Comparing cohorts with randomised trials

Randomised trials are experimental cohorts, because we follow them up, forward in time, to detect incident events of interest and associate them to the exposure, which in this case is the prescribed intervention. They therefore have a similar design to observational cohorts, in which incidence of a particular event in the exposed group is compared with that in the non-exposed. However, the fundamental difference is that the investigator has control over and determines who gets the intervention in randomised trials by randomizing the exposure while in observational studies, he/she only observes individuals or groups that have selected themselves into various exposure groups. For ethical issues, we cannot intentionally expose a group of people to a putatively harmful substance (e.g. a suspected carcinogen) simply because we want to study an association. The "exposure" in most randomised trials therefore is a theorized "treatment" or "preventive measure". Secondly, in observational cohorts, exposure is circumstantial and cannot be randomly allocated. . Lack of randomization in observational cohorts makes causal inference more difficult than in well conducted randomized trials. If an increased risk of a certain disease tends to be found in workers at a certain chemical factory, and these workers tend to live in a particular labour-line, the labour line environment cannot be ruled out as the possible source of the disease vis-à-vis the chemical factory. Therefore, the fact that we can randomly allocate individuals to exposures in the experimental cohort makes randomised trials the most powerful tool in epidemiological inquiry.

c. Objectives of Interventional Trials

The objectives of an interventional or experimental trial are to:

- Evaluate new approaches to treatment and prevention, thus the concept of therapeutic and preventive trials.
- Evaluate tests of new health and medical care technology
- Assess new programs for screening and early detection of disease
- Assess new ways of organizing and delivering health care services

d. Types of Intervention Trials

There are 2 broad types of intervention trials: clinical trials and community trials.

Lesson 2: Clinical Trials and Community trials

Lesson Outline

a. *Clinical trials*
b. Community trials
c. Analysis of experimental studies

Lesson Objectives:

By the end of this session, the MPHO should be able to:

1. Outline and distinguish the phases of clinical trials
2. Describe the key issues in setting up a clinical trial
3. Illustrate the key issues in the conduct of a clinical trial
4. Describe the key characteristics of a community trial
5. Choose appropriate methods for analysing the outcomes of interventional studies

a. Clinical Trials

Introduction: We define clinical trial as a research activity or an experiment that involves the administration of a test regimen to humans to evaluate its efficacy and safety. In this experiment the unit of randomization is the individual and the site of the trial is usually a clinic or a hospital ward. A community trial is an experiment in which the unit of allocation is a cluster of individuals or an entire community. Clinical or community trials can be either therapeutic or preventive depending on the intervention being evaluated.

1. Phases of Clinical Trials

Phase I trials: The objective of a phase I trial is to study the safety, pharmacological profile and the mode of action of a new drug or vaccine. It may also include studies of the dose and route of administration. Phase I trials involve small numbers of individuals, usually 30 to 50 subjects. The duration is usually 18 – 24 months.

Phase II trials: In this phase the focus is on demonstration of safety and limited efficacy for drugs or safety and Immunogenicity for vaccines. Phase II trials typically involve between 200 – 500 participants and last 18 – 24 months. Subjects are usually randomly allocated to study and control groups.

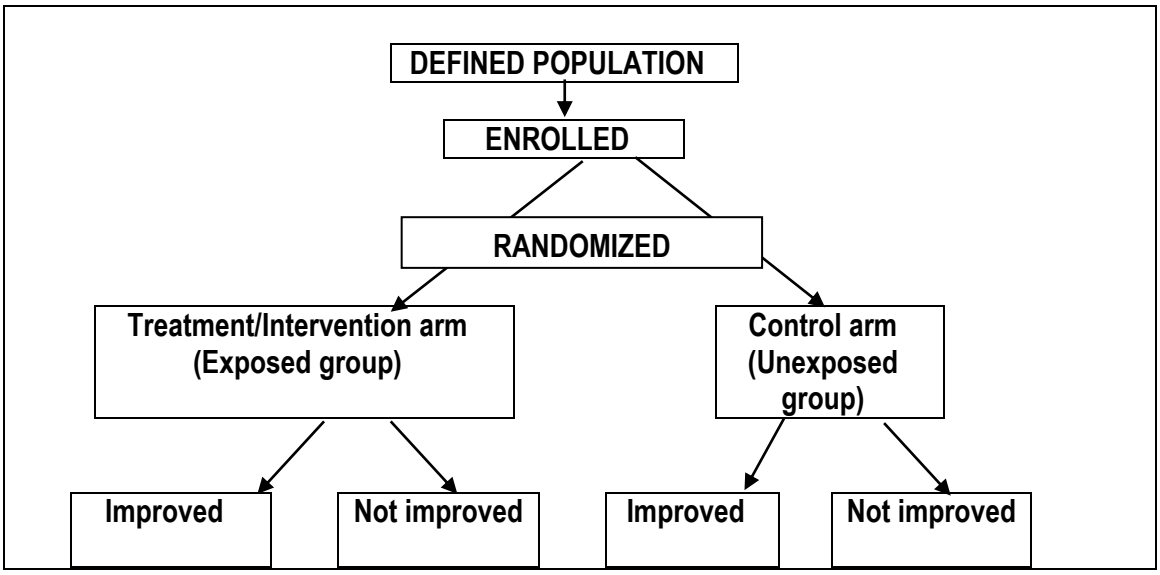
Phase III trials: The objective of a phase III trial is a complete assessment of safety and efficacy. It involves large numbers, usually in the thousands or tens of thousands and study subjects must be randomly allocated to study and control groups. These trials take 3 – 5 years and may be multi-centre trials. They are also called Field Trials or Community Trials.

Phase IV trials: This phase is conducted after the drug or vaccine has been licensed for distribution or marketing and is in use within the population. The objective of this phase is pharmaco-vigilance to establish the incidence of adverse reactions and the effect of long-term use of the product. This phase studies the effectiveness of the product i.e. the extent to which the product does what it is intend to do when deployed in field conditions

2. Design Overview

As the figure below shows, randomised, double blind controlled study is the ideal design for evaluating the efficacy and side effects of new forms of interventions. It is said to be the ultimate in

clinical research design and is thus a very powerful research tool. The design of the study is inherent in its name. The key aspects of the design are discussed below:



3. Selection of trial participants

The study population should be selected in such a way that the findings of the trial can be applied to a reference population (external validity) and that the observed differences between the study groups can only be attributed to the hypothesized effect under investigation (internal validity). The criteria for deciding who will or will not be included in the trial must be clearly agreed upon and spelt out as inclusion and exclusion (eligibility) criteria. These criteria should be written down clearly as part of the research protocol. Individuals who fulfil eligibility criteria for inclusion into the study must have an informed consent administered prior to enrolment. Other rights of study human subjects must be taken care of at this stage also. Issues of informed consent and other rights of subjects have recently received a great deal of attention as absolute pre-requisites to ethically sound research. A detailed discussion of these issues can be found in the section on ethics in research, which is part of your course.

Sample size and power considerations are very important in designing an intervention trial. In order to be able to draw conclusions from the study sample it is important that a trial must have a sufficient sample size to have adequate statistical power or ability to detect reliably a small to moderate but clinically important difference between treatment groups that are most likely to occur. Statistical power depends on, sample size, the total number of end points experienced by the study population as well as the difference in compliance between the treatment groups.

4. Assignment of trial participants to treatment groups - Randomisation

Allocation of trial participants to treatment group can be by random or non-random assignment. Randomisation is the hallmark of a clinical trial. It is defined as the process of assigning trial participants to treatment group using an element of chance to determine the assignments in order to reduce bias. Random assignment involves more than just alternate assignment or a flip of a coin. Traditionally, a table of random numbers or computer-generated random numbers are utilized. Randomization may be simple or restricted (blocked, matched or stratified). Additionally, randomization could be of individuals or groups e.g., villages, schools etc (see community trials). In a well-randomised scheme, the next assignment is unpredictable and solely controlled by chance.

Randomisation has several advantages:

- Non-predictability of the next assignment hence eliminating bias in subject allocation
- Avoid subjective bias of the investigators that may be introduced into the process of selecting patients for one treatment group over another
- Increase likelihood that the groups will be comparable with regard to baseline characteristics except the intervention under study
- Control for potential confounders (both known and unknown)

Although randomisation attempts to achieve comparability on baseline characteristics, it is not a guarantee that this will happen. This is because by chance alone some factors may still be differentially distributed.

5. Concealing the allocation- Blinding

Concealing the allocation to the treatment groups is important so as to reduce bias in assessing treatment outcomes. If either the investigator or the subject or the assessor is aware of the treatment group of the study participant it may influence his assessment or interpretation of the treatment outcome in an intervention trial. Masking or blinding can achieve concealing the allocation. We use a code that is only broken after the analysis. Four types of blinding are possible:

1. *Open Label:* Everyone i.e. the subjects, the investigators and the assessors know who is in which treatment group.
2. *Single Blind:* Either the subject or the investigators are unaware of the treatment group.
3. *Double Blind:* Either the subjects and the investigators or the subjects and the assessors are unaware of the treatment group.
4. *Triple Blind:* Everyone i.e. the subjects, the investigators and the assessors are unaware of treatment group.

One way of blinding is by using a ***placebo***, which may be an inert substance that looks, tastes and smells like the active agent under investigation. The mode of administration of a placebo, its dosage regimen and shape should also be similar to the active agent. Often a placebo is difficult to obtain or manufacture. Moreover use of a placebo does not guarantee blinding. In situations where standard treatment for the condition under study exists, it should be used in place of a placebo otherwise the research shall be deemed unethical.

A placebo effect is the perceived beneficial effect reported by individuals on a placebo due to the expectation that any medication will have an effect.

6. Follow up of Subjects Enrolled in an Intervention Trial

In an intervention trial it is essential to develop a follow up scheme so as to collect information on key variables of interest. These include:

- **Compliance with the follow up scheme:** Study participants who do not return for follow up visits may be different from those who do. Loss to follow up should be kept to a minimum.
- **Crossovers:** Crossovers can be **planned** in which subjects for a new intervention act as their own control and are deliberately switched to another therapy after assessing one. Such designs have the problem of the carry-over effect in which the therapeutic effect of the first treatment might still be present. There is therefore a need for an adequate washout period. In addition, we risk having psychological responses. The design is also not possible if there is definitive cure by the first therapy (e.g. a surgical procedure). **Unplanned** crossover may also occur, in which the subjects switch their medication, or in which a subject must be switched due to non-response or side effects from a particular regime

- **Adherence with the assigned treatment:** Some subjects may deviate from assigned medications due to side effects, forgetting to take medication, withdrawing consent, seeking other treatment on their own, worsening disease
- **Outcome information:** This may be improvement in clinical condition (desired) or side effects (undesired). It is important that ascertainment of outcome is performed comparably in the treatment groups. The outcome should not be measured more carefully in those receiving the intervention than in those receiving the control drug or substance or measure. Blinding helps try to eliminate this bias.
- **Monitoring Safety in a clinical trial:** It is important to put in place mechanisms for monitoring the data from a clinical trial as it accrues. In large or multi-centre studies, a Data and Safety Monitoring Board (DSMB) usually does this. It is a group of eminent independent researchers whose role is to carefully monitor trial data for any safety concerns. Termination of a trial may be considered if there are adverse events that endanger the safety of trial participants. Similarly, a trial may be terminated if there is a sustained statistical association that is very extreme and highly significant is observed.

b. Community Trials (Field trials/Intervention trials)

Design of a Community trial: As mentioned above, a community trial is an experiment in which the unit of allocation is a cluster of individuals or an entire community. Community trials can be either therapeutic or preventive depending on the intervention being evaluated. Apart from the difference in randomisation other aspects of the design and implementation of community trials are very similar to clinical trials. Communities may be randomly allocated to interventions, as groups (group randomisation)

Facts about Community Trials

- Community trials are experimental studies in which the treatment groups are communities and not individuals
- Community trials are suitable when the disease being studied has its origins in social conditions, which in turn can most easily be influenced by interventions directed at group behaviour as well as at individuals
- One limitation is that only a small number of communities can be included
- Random allocation of communities may not always be practical
- In community trials, it is often difficult to separate out intervention effect from other effects such as that of general social changes taking place

Examples of Community Trials

Fluoridation Trials

A number of years ago, it was observed that residents of areas with water that was naturally high in fluoride had considerably less dental caries than residents of low-fluoride areas. Shortly thereafter, trials to test the prophylactic effectiveness of artificial fluoridation of water were proposed. Several pairs of neighbouring communities were chosen, all with a naturally low level of fluoride in the drinking water. Following baseline measurements of fluoride content and of dental caries, the water of one community in each pair was left unchanged while the other was treated by addition of approximately 1 part per million (ppm) of fluoride.[Refer to Leon Gordis: Epidemiology ; 3rd Edition, pages 8-9]

EXERCISE 2.4.1

1. What intervention was being tested?
2. Is there any comparison group? If yes, which one is it?

3. What was the use of conducting baseline measurements of fluoride content and dental caries?
4. Describe the randomisation scheme used? What is your comment on this randomisation scheme?
5. What do you think was the duration of follow up?
6. What outcome information do you think was collected?

Cardiovascular trial

Attempts to lower the incidence and mortality from cardiovascular disease were exemplified by the Stanford Three-Community survey. In this study, three communities were selected: two were experimental communities, the third a control community. A profile including age, plasma cholesterol concentration, and systolic blood pressure, smoking history, relative weight and ECG findings was the basis for classifying individuals as "high risk". One of the two experimental communities received personal counselling for high-risk individuals; the other community received only messages through public media. Findings showed significant reduction in consumption of saturated fat and cholesterol for both communities, with a greater amount of change in the population that received intensive individual instruction.

Exercise 2.4.2

1. Describe the intervention in the two experimental communities?
2. What was done to the control community?
3. What were the outcome measurements?

The Rakai STD Control for AIDS Prevention Study:

In 1994 investigators working with the Rakai Project conducted a community-based, randomised, controlled, single-blinded trial. The trial was designed to test the following hypotheses:

- Intensive STD control will result in reduced HIV acquisition and transmission at a population level
- Intensive STD control can be achieved rapidly and effectively by a mass treatment strategy

2.4.3 Exercise

Review the attached case study of the Rakai STD Control for AIDS Prevention; Study and respond to the accompanying questions.

c. Analysis of experimental studies

There are several approaches to the analysis. They include:

1. **Risk** (**Relative risk and Odds ratios):** In dichotomous outcomes in which time is not considered, we may compute the relative risk and Odds ratios. Incidences are then often expressed as person years of observation.
2. **Rates** (Rate Ratios)
3. **Efficacy:** Used especially in vaccine trials. It is denoted by:

$$\text{Efficacy} = \frac{(\text{Rate in un-treated}) - (\text{Rate in treated})}{(\text{Rate in untreated})} \times 100$$

4. **Failure time methods and survival analysis:** These put into consideration the time to a particular outcome because in some cohort studies, it may not be possible to wait for the entire

population indefinitely. We use survival and hazard analysis. [These techniques will be discussed in the module: Applied Epidemiology II]
5. **Others:** Other techniques include calculating the “number needed to treat” and “number needed to harm”.

In community trials, we often conduct a baseline survey at the start of the intervention, and a survey after the intervention, depending on the nature of the outcome we are evaluating.

Lesson 3: Introduction to Ethics in Research

Introduction: The conduct of research especially that involving human beings and that involving the prescription of an intervention raises a number of ethical issues. These issues will be introduced in this lesson. [The subject of ethics is however a broad one. It will be covered extensively in another module – Health Ethics and Law]

Lesson Outline

a. Importance of ethics in research
b. Fundamental principles in research ethics

Lesson Objective: By the end of this lesson, the MPHO should be able to apply the fundamental ethical principles in the conduct of epidemiological research.

a. Importance of ethics in research

Research participants are essential to the conduct of research, enabling researchers to make progress and discoveries in the fields of medicine and health. As such, the relationship between researchers and participants is critical and should be based on accurate information, trust, and respect. It is thus important to understand the principles governing the ethical conduct of research in human beings so as to protect their rights as research participants. History is full of evidence of unethical research conducted in human beings. It is this history that has led to the development of guidelines and regulations that govern the conduct of research.

ACTIVITY 2.4.2

Review the following historical events in research

- The Nuremberg Doctors trial (1946)
- The Thalidomide Tragedy (1960)
- The Tuskegee Syphilis study (1972)

Briefly review the following international guidelines and regulations regarding research in human subjects

- Nuremberg code
- Declaration of Helsinki
- Belmont report
- Common rule
- CIOMS (Council for the International Organization of Medical Sciences)
- International Conference on Harmonization

In 1979, the United States National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research wrote the report entitled *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, commonly called the "Belmont Report." In this report, the Commission identified and described the basic ethical principles that underlie research. The Commission considered the boundaries between biomedical and behavioural research and the accepted and routine practice of medicine in order to "know what activities ought to undergo review for the protection of human subjects of research." The report also describes the assessment of risk/benefit criteria in the determination of appropriateness of research on participants, appropriate guidelines for this assessment, and the nature and definition of informed consent.

b. Fundamental principles in research ethics

The three fundamental ethical principles that guide the ethical conduct of research involving human participants are:

(1) **Respect for Persons (autonomy)**
(2) **Beneficence**
(3) **Justice**

1. Respect for Persons: The principle of respect for persons incorporates at least two ethical standards:

One: Individuals should be treated as autonomous agents.

"An autonomous person is an individual capable of deliberation about personal goals and of acting under such deliberation. To respect autonomy is to give weight to the autonomous person's considered opinions and choices while refraining from obstructing his or her actions..." (Belmont Report)

Prospective research participants must be given the information they need to determine whether or not to participate in a study. There should be no pressure to participate and ample time to decide. Respect for persons demands that participants enter into the research voluntarily and with adequate information. This is called *informed consent*.

Two: Persons with diminished autonomy may need additional protections.

Special provision may need to be made when comprehension is severely limited or when a class of participants is considered incapable of informed decision-making (such as with children or people with severe developmental disorders or dementias). Even for these persons, however, respect requires giving them the opportunity to choose, to the extent they are able, whether or not to participate in research activities. In some cases, respect for persons may require seeking the permission of other parties, such as a parent or legal guardian. The judgment that someone lacks autonomy should be periodically re-evaluated and may vary in different situations.

2. Beneficence: Human participants are treated in an ethical manner not only by respecting their decision and protecting them from harm, but also by making efforts to secure their well-being. The principle of *beneficence* obligates the researcher to maximize possible benefits and minimize possible harm.

The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite inherent harms or risks. Balancing risks and benefits is an important consideration. The goal of much research is societal benefit; however, in the interest of securing societal benefits; no individual shall be intentionally injured.

3. Justice: The ethical considerations of risks versus benefits lead to the question of *justice*. This principle requires that participants be treated fairly and involves questions such as: Who should bear the risks of research, and who should receive its benefits?

Justice is a difficult and complex ethical issue. Attempts must be made at all times in a study to distribute the risks and benefits fairly and without bias. Also, unless there is clear justification, research should not involve persons from groups that are unlikely to benefit from subsequent applications of the research. The concept of justice may be questioned when deciding who will be given an opportunity to participate, which people will be excluded, and the reasons for exclusion. When making such decisions, the researcher must ask: Are some classes of persons being selected simply because of their availability, their compromised position, or their vulnerability-rather than for reasons directly related to the problem being studied?

ACTIVITY 2.4.3
Review the attached case studies on ethics and respond to the accompanying questions.

ESSENTIAL READING

1. Designing Clinical Research, 2nd edition. Hulley SB, et al. Lippincott, Williams, and Wilkins, Philadelphia. 2001.
2. Gordis L. (1996): *Epidemiology.* W.B. Saunders Company, Philadelphia. Chapters 6 & 7.
3. Last J. (1988). *Dictionary of Epidemiology.* Second Edition. Oxford University Press, Oxford.
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5. Wawer M, Gray R, Sewankambo N, et al. A randomized, community trial of intensive sexually transmitted disease control for AIDS prevention, Rakai, Uganda. *AIDS* 1998, 12(10): 1211-25.
6. Wawer MJ, Sewankambo NK, Serwadda D, Quinn TC, Paxton LA, Kiwanuka N, Wabwire-Mangen F, Li C, Lutalo T, Nalugoda F, Gaydos CA, Moulton LH, Meehan MO, Ahmed S, Rakai Project Study Group, Gray RH. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomized community trial. *Lancet* 1999; 353:525-35.

2.4.7 Extension Activities

Extension Activity 1 : Discussion Forum Question

NO FORUM QUESTION

Extension Activity 2: Self- Assessment Quiz

QUIZ 2.4.1

(Choose one correct option)

1. Choose the most incorrect statement regarding a specific study design
   a) Manipulation of the environment factors is essential in all observational study designs
   b) Randomisation is an essential element in experimental studies
   c) Randomisation is not necessary for an investigator to get valid results in experimental study designs
   d) Only A and C

2. Select the most incorrect statement
   a) Excessive control of study conditions in experimental studies can actually be an advantage
   b) Randomisation of subjects in experimental studies may at times not be feasible
   c) The investigator is not able to isolate observed effect of the study factor in an experimental study design
   d) Double blinding is recommended for all experimental studies

3. Choose the most correct statement:
   a) The quasi-experimental study designs are the best suited to investigate and measure exposure and disease at the same time
   b) Ecological study designs, unlike cohort studies, are suited for etiological hypotheses
   c) Cross-sectional studies cannot produce analytical data
   d) Temporal relationship is best shown in cohort studies

4. The main purpose of random assignment in a clinical trial is to:
   a) Help ensure that study subjects are representative of the general population
   b) Facilitate double blinding
   c) Increase external validity
   d) Try to have the study groups comparable on baseline characteristics

e) Reduce selection bias in allocation of treatment

5. The essential difference between experimental and observational studies is that in experimental investigations

a) The study and control groups are equal in size
b) The study is prospective
c) The study and control groups are always compatible
d) The investigator determines who shall be exposed to the suspected factor and who shall not
e) Controls are used

3.0 ADDITIONAL RESOURCES

3.1 TEXT DOCUMENTS FOR ADDITIONAL READING

Text Document 3.1.1: THE EVOLUTION OF EPIDEMIOLOGY

An extract from Principles of Epidemiology, CDC Training Manual 1992, Page 4-5

Although epidemiological thinking has been traced from Hippocrates (circa 400 B.C.) through Graunt (1662), Farr, Snow (both mid-1800's, and others, the discipline did not blossom until the end of the Second World War. The contributions of some of these early and more recent thinkers are described below. Hippocrates (circa 400 B.C.) attempted to explain disease occurrence from a rational instead of a supernatural viewpoint. In his essay entitled "On Airs, Waters, and Places," Hippocrates suggested that environmental and host factors such as behaviours might influence the development of disease.

Another early contributor to epidemiology was John Graunt, a London haberdasher who published his landmark analysis of mortality data in 1662. He was the first to quantify patterns of birth, death, and disease occurrence, noting male-female disparities, high infant mortality, urban-rural differences, and seasonal variations. No one built upon Graunt's work until the mid-1800, when William Farr began to systematically collect and analyse Britain's mortality statistics. Farr, considered the father of modern vital statistics and surveillance, developed many of the basic practices used today in vital statistics and disease classification. He extended the epidemiological analysis of morbidity and mortality data, looking at the effects of marital status, occupation, and altitude. He also developed many epidemiological concepts and techniques still in use today.

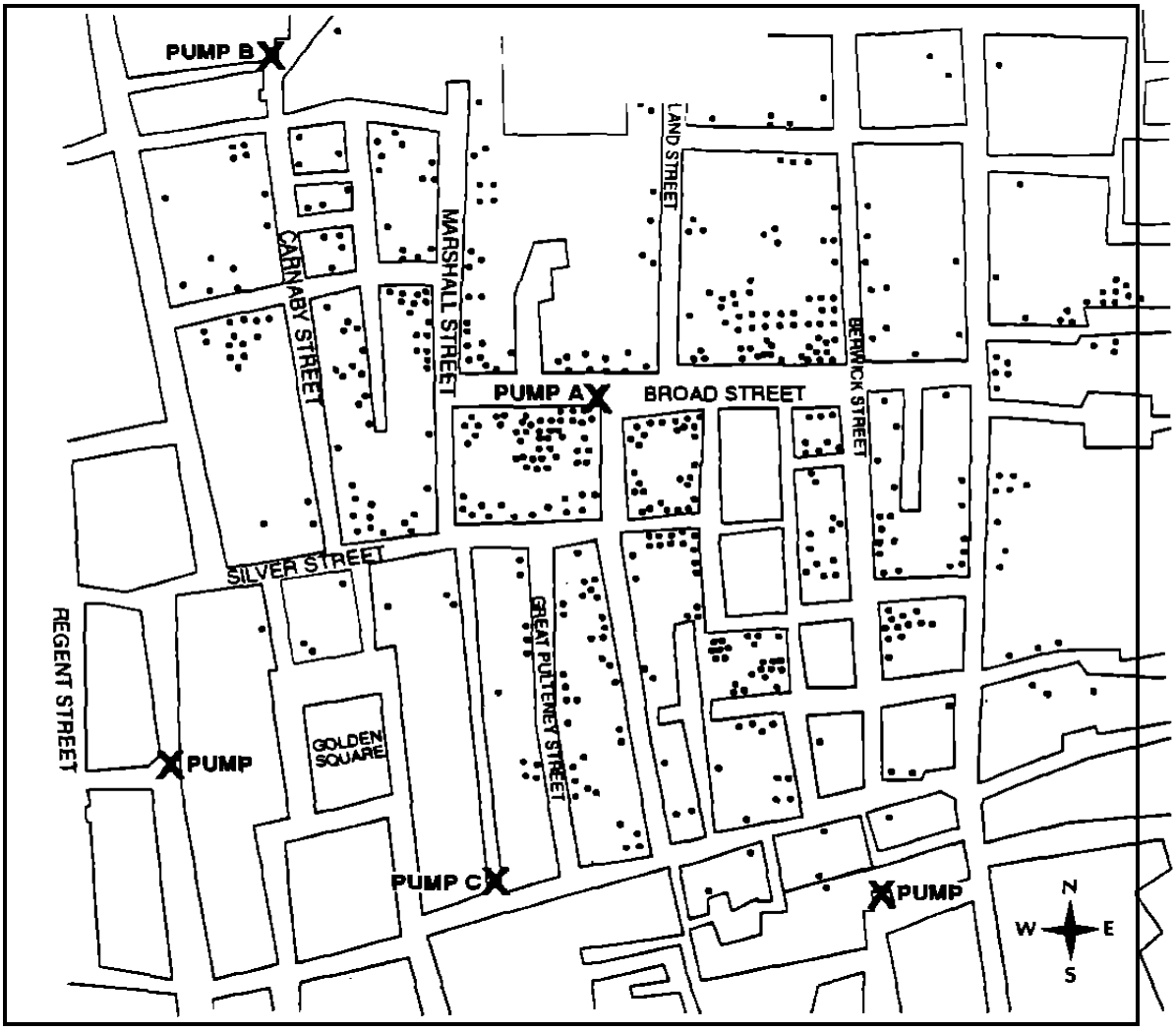
Meanwhile, an anaesthesiologist named John Snow was conducting a series of investigations in London that later earned him the title "the father of field epidemiology." Twenty years before the development of the microscope, Snow conducted studies of cholera outbreaks both to discover the cause of disease and to prevent its recurrence. Because his work classically illustrates the sequence from descriptive epidemiology to hypothesis generation to hypothesis testing (analytic epidemiology) to application, we will consider two of his efforts in detail. Snow conducted his classic study in 1854 when an epidemic of cholera developed in the Golden Square of London. He began his investigation by determining where in this area persons with cholera lived and worked. He then used this information to map the distribution of cases on what epidemiologists call a spot map. His map in shown in Figure 1.1

Because Snow believed that water was a source of infection for cholera, he marked the location of water pumps on his spot map, and then looked for a relationship between the distribution of cholera case households and the location of pumps. He noticed that more case households clustered around Pump A, the Broad Street pump, than around Pump B or C, and he concluded that the Broad Street pump was the most likely source of infection. Questioning residents who lived near the other pumps, he found that they avoided Pump B because it was grossly contaminated, and that Pump C was located too inconveniently for most residents of the Golden Square area. From this information, it appeared to John Snow that the Broad Street pump was probably the primary source of water for most persons with cholera in the Golden Square area. He realized, however, that it was too soon to draw that conclusion because the map showed no cholera cases in a two-block area to the east of the Broad Street pump. Perhaps no one lived in that area. Or perhaps the residents were somehow protected.

Upon investigating, Snow found that a brewery was located there and that it had a deep well on the premises where brewery workers, who also lived in the area, got their water. In addition, the brewery allotted workers a daily quota of malt liquor. Access to these uncontaminated rations could explain why none of the brewery's employees contracted cholera. To confirm that the Broad Street pump was the source of the epidemic, Snow gathered information on where persons with cholera had obtained their water. Consumption

of water from the Broad Street pump was the one common factor among the cholera patients. According to legend, Snow removed the handle of that pump and aborted the outbreak.

Fig 1.1: Distribution of cholera cases in the Golden Square area of London, August—September 1854



Snow's second major contribution involved another investigation of the same

Snow's second major contribution involved another investigation of the same outbreak of cholera that occurred in London in 1854. In a London epidemic in 1849, Snow had noted that districts with the highest mortalities had water supplied by two companies: the Lambeth Company and the Southwark and Vauxhall Company. At that time, both companies obtained water from the Thames River, at intake points that were below London. In 1852, the Lambeth Company moved their water works to above London, thus obtaining water that was free of London sewage. When cholera returned to London in 1853, Snow realized the Lambeth Company's relocation of its intake point would allow him to compare districts that were supplied with water from above London with districts that received water from below London. Table 1.1 shows what Snow found when he made that comparison for cholera mortality over a 7-week period during the summer of 1854.

TABLE 1.1
Mortality from cholera in the districts of London supplied by the Southwark and Vauxhall and the Lambeth Companies, July 9 - August 26, 1854

Districts with Water Supplied by	Population (1851 Census)	Deaths from Cholera	Cholera Death Rate per 1,000 Population
Southwark and Vauxhall Co. only	167,654	844	5.0
Lambeth Co. only	19,133	18	0.9
Both companies	300,149	652	2.2

The data in Table 1.1 show that the risk of death from cholera was more than 5 times higher in districts served only by the Southwark and Vauxhall Company than in those served only by the Lambeth Company. Interestingly, the mortality rate in districts supplied by both companies fell between the rates for districts served exclusively by either company. These data were consistent with the hypothesis that water obtained from the Thames below London was a source of cholera. Alternatively, the populations supplied by the two companies may have differed on a number of other factors that affected their risk of cholera.

To test his water supply hypothesis, Snow focused on the districts served by both companies, because the households within a district were generally comparable except for water Supply Company. In these districts, Snow identified the water supply company for every house in which a death from cholera had occurred during the 7-week period. Table 1.2 shows his findings. This further study added support to Snow's hypothesis, and demonstrates the sequence of steps used today to investigate outbreaks of disease. Based on a characterization of the cases and population at risk by time, place, and person, Snow developed a testable hypothesis. He then tested this hypothesis with a more rigorously designed study, ensuring that the groups to be compared were comparable. After this study, efforts to control the epidemic were directed at changing the location of the water intake of the Southwark and Vauxhall Company to avoid sources of contamination. Thus, with no knowledge of the existence of microorganisms, Snow demonstrated through epidemiological studies that water could serve as a vehicle for transmitting cholera and that epidemiological information could be used to direct prompt and appropriate public health action.

In the mid- and late-1800's, many others in Europe and the United States began to apply epidemiological methods to investigate disease occurrence. At that time, most investigators focused on acute infectious diseases. In the 1900's, epidemiologists extended their methods to noninfectious diseases. The period since the Second World War has seen an explosion in the development of research methods and the theoretical underpinnings of epidemiology, and in the application of epidemiology to the entire range of health-related outcomes, behaviors, and even knowledge and attitudes. The studies by Doll and Hill linking smoking to lung cancer and the study of cardiovascular disease among residents of Framingham, Massachusetts, are two examples of how pioneering researchers have applied epidemiological methods to chronic disease since World War II. Finally, during the 1960's and early 1970's health workers applied epidemiological methods to eradicate smallpox worldwide. This was an achievement in applied epidemiology of unprecedented proportions. Today, public health workers throughout the world accept and use epidemiology routinely. Epidemiology is often practiced or used by non-epidemiologists to characterize the health of their communities and to solve day-to-day problems. This landmark in the evolution of the discipline is less dramatic than the eradication of smallpox, but it is no less important in improving the health of people everywhere.

TABLE 1.2
Mortality from cholera in London related to the water supply of individual houses in districts served by both the Southwark and Vauxhall Company and the Lambeth Company, July 9 - August 26. 1854

Water Supply of Individual House	Population (1851 Census)	Deaths from Cholera	Death Pate per 1,000 Population
Southwark and Vauxhall Co	98,862	419	4.2
Lambeth Co.	154,615	80	0.5

3.2 GLOSSARY OF TERMS

Agent: A factor, such as a microorganism, chemical substance, or form of radiation, whose presence, excessive presence, or (in deficiency diseases) relative absence is essential for the occurrence of a disease. A disease may have a single agent, a number of independent alternative agents (at least one of which must be present), or a complex of two or more factors whose combined presence is essential for the development of the disease.

Blinding/Masking: A procedure in which one or more parties to the trial are kept unaware of assignment to treatment group. Double blind: neither volunteer(s) nor the investigator(s), monitor or data analyst know the assignment. The purpose of blinding is to eliminate bias in assessing treatment outcomes.

Environment: All that which is external to the individual human host; can be divided into physical, biological, social, or cultural, any or all of which can influence health status of populations.

Host: A person or other living animal, including birds and arthropods that afford subsistence or lodgment to an infectious agent under natural conditions.

Immunity: It refers a host state in which the host is able to protect itself from invasion by disease causing organisms. Immunity can be natural or acquired.

Inference: It is the process of passing from observations and axioms to generalizations. Epidemiological inquiry often starts with the observation of factors, to assess whether they are related to a particular condition. We then use analytical techniques and criteria to ascertain causation and generalize to populations. In statistics, we generalize sample data to populations, usually with calculated degrees of uncertainty.

Natural History: The natural history of a disease is defined as its usual trend of progress from its inception to its resolution, and the factors influencing this.

Placebo: A pharmacologically inert substance or a substance with no active ingredient that is used to mimic treatment in experimental studies

Randomisation: The process of assigning trial participants to treatment group using an element of chance to determine the assignments in order to reduce bias.

Risk factor: An aspect of personal behaviour or life-style, and environmental exposure, or an inborn or inherited characteristic, that, on the basis of epidemiological evidence, is known to be associated with health-related condition(s) considered important to prevent

Susceptibility: It refers to the state in which the host is unable to protect itself from invading disease causing agents

3.3 REFERENCES

1. *Epidemiology* by Leon Gordis 2nd Edition
2. *Epidemiology in Medicine* Charles H. Heinekens and Julie E. Burring
3. *Dictionary of Epidemiology* by John M Last
4. *Principles of Epidemiology*, The Centers for Disease Control and Prevention Training Manual 1992

3.4 ANSWERS TO QUIZ QUESTIONS

QUIZ 2.1.1

1.d 2.a 3.b 4.d 5.c

QUIZ 2.2.1

1.c 2.a 3.c 4.a 5.c 6.b 7.c 8.a 9.b 10.c 11.c 12.d
13.d 14.c 15.a 16c 17.a

QUIZ 2.3.1

1.c 2.a 3.c 4.c 5.b 6.c 7.c 8.b 9.b 10.d 11.d 12.a
13.a 14.b 15.b 16d

QUIZ 2.4.1

1.d 2.c 3.d 4.e 5.d

3.5 INDEX OF URLs FOR INTERNET RESOURCES

1. www.cdc.gov/eis/casestudies/XscreeningHIV.student.871-703.pdf : CDC – Epidemiology Programme Office: Case studies in applied epidemiology No. 871-703. **Screening for antibody to HIV** – Students' Guide [Application of validity]

2. en.wikipedia.org/wiki/epidemiology: Visit this online dictionary to obtain additional information on the key concepts in Epidemiology

3.6 INDEX OF DISCUSSION FORUM QUESTIONS

You are encouraged to participate in the discussion forums that have been pre-planned for you in the semester. Through these forums, you will be able to exchange information with the moderators and fellow students and gain a deeper understanding of the material you have read. There will be at-least one discussion forum for each course, with a number of questions drawn from each course unit. You are requested to post your discussion points to the board for other members to share. Please be brief and to the point. You may discuss only one question or a number of them depending on where you feel motivated. You may also post a discussion point that is outside the set questions, provided you have **HOT** points to share. These forums will enhance the "virtual" classroom environment and facilitate you to learn at the same pace as the others.

There is a detailed outline of the schedule of these forums that will be handed to you at the beginning of the semester, under the resource: **SEMESTER SCHEDULES**. At the precise times indicated (Modifications in the schedule may from time to time be communicated to you by the Moderator), the discussion will be activated and you will be called upon to contribute; this will be a "silent" online call – you are requested to remain alert, and regularly check the forum platform or your internet mail-box for the call. For each course the discussion will run for an entire week.

The forums will either be hosted at the Makerere University School of Public Health Distance learning site on either: http://courses.musph.ac.ug or http://musk.musph.ac.ug . Please sign up and register your unique identity in the forum. The following is a summary of the questions that are up for discussion in the Discussion Forum for this particular Course:

1. *With a specific citation, discuss how any one historical milestone is linked to the development of the "Epidemiological Approach".*

2. *Descriptive Epidemiology covers several areas that include: Measurement of Disease, Standardisation of Rates, Validity and Reliability of Measurements, Principles of Disease Surveillance and Outbreaks and Descriptive Study designs; For this forum, we shall focus on validity of measurements – Briefly Describe some measures of validity and how they can be applied to selection of screening tests for different purposes*

3. *Analytical Epidemiology includes Cohort studies, Case-control studies, Assessment of Risk as well as Causal inference. For this forum, we shall focus on analytical study designs. What key features distinguish the Case-Control Studies from Cohort studies their advantages and disadvantages*

POST YOUR REPLY NOW:

Post your reply **now** to one or more of these issues and attend the Forum; you will discover the unique learning experience from sharing knowledge in this interesting resource!

3.7 INDEX OF ADDITIONAL RESOURCES FOLDER

1. Exercises in outbreak investigation
2. Exercises in disease surveillance
3. Worked example on a food-poisoning outbreak
4. Exercises on application of validity (PDF)
5. Evaluating diagnostic tests
6. Exercises in counting diseases
7. Principles of Epidemiology
8. Disease Surveillance
9. Standardisation of Rates
10. UNEPI Diseases Surveillance Manual
11. Using Epi Info in Field Epidemiology
12. Worked Example on Standardisation of rates

3.8 INDEX OF SELECTED REAL TIME LECTURE NOTES

1. Disease surveillance
2. Introduction to Epidemiology
3. Outbreaks and Outbreak investigation
4. Standardisation of Rates
5. Validity and Reliability

3.9 SUMMATIVE EVALUATION OF THE INSTRUCTION PROCESS

Summative Evaluation of the instruction will be conducted using the following means:

1. Progressive Assessment in form of Hand-in Assignments
2. The University Examination
3. An optional Post-test
4. A Course Post Evaluation Questionnaire

Progressive Assessment – Hand-in Assignments

These assignments should be handed in by the time of sitting for the progressive assessment test at the institute of public health. They will be marked and will contribute to the final progressive score. The number, nature and timing of assignments will be determined by the Course Coordinator. Some of these assignments may be directly included in these materials by the Course Coordinator. An index of them is listed below:

	TITLE	COMENTS
1.		
2.		
3.		
4.		
5.		

Post-test

It is optional for you to attempt the **Post-test**. It will assist you to gauge your grasp of the material after the instruction process. The test **may be** contained in the **Additional Resources Folder**.

Post Evaluation

We are in need of your feedback on the quality and content of these materials. It will be valuable to the iterative process of their further improvement. For this purpose, we have attached a questionnaire to gauge your perception of the design and conduct of this course and to link this to your understanding of the subject matter. This questionnaire has been introduced to you previously. It contains two parts: a Post Evaluation of the materials for the previous semester and a pre-evaluation of the materials you expect for this semester. Please note that this is not a progressive assessment or exam, and will not contribute to your final mark. It should be completed at the beginning of the semester. Please fill in the Evaluation questionnaire for this semester; make comments as requested, and send it as an e-mail attachment or hardcopy to: **Dr. Roy William Mayega – Instructional Designer/Editor – MPH Distance education Programme:** e-mail: de_materials@musph.ac.ug .