

Clinical epidemiology. Modern principles and rules conducting of clinical researches. Concept of a zero hypothesis, principles of randomization and stratification in medical researches.

## Epidemiology of Chronic Non-communicable Diseases and Conditions

### Epidemiology

Epidemiology is 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.”

To put it more simply, epidemiology is the task of using data to answer questions of:

Who is getting sick?

What is making people sick? And,

How can we use this information to reduce the risk of others getting sick?

Without quality health data, it is very difficult to answer these questions. A surveillance system that serves to collect health data in a complete and timely manner is thus essential to the practice of epidemiology.

### Surveillance

Surveillance is defined as “the ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in planning, implementation, and evaluation of public health practice.”

Data collected in a surveillance system can be used for many purposes, including:

To estimate the magnitude of a health problem in a population

To understand the natural history of a disease

To detect outbreaks or epidemics

To document the distribution of a health event

To test hypotheses about causes of disease

To monitor changes in infectious organisms

### Types of Surveillance

Communicable diseases are those that can be transmitted from person to person (or animal to human) via direct contact with body fluids, ingesting contaminated food or water, inhalation of contaminated air, or the bite of an infected insect. Bacteria, viruses, and parasites are some of the organisms that can cause communicable diseases. Examples of communicable diseases are Hepatitis B, Salmonellosis, Measles, and West Nile Virus.

Preventing and controlling communicable disease is a necessary and critical aspect of assuring community health, and is an affirmative duty of local public health departments. Protecting the public's health from communicable disease threats requires a proactive public health disease surveillance system, timely epidemiological assessment, and ongoing disease prevention education.

Because community disease surveillance and control is a critical component of disease prevention, the Kent County Health Department monitors the occurrence of specific diseases on a community-wide basis. Physicians, laboratories, and schools all report cases of disease to the Health Department. With this information, we are able to monitor both the incidence (number of new cases) and prevalence (number of existing cases) of disease in Kent County.

Four primary types of epidemiology studies.

The “Big Picture”

In Michigan, the state Public Health Code requires that healthcare providers (physicians, physician assistants, pharmacists, dentists, nurses, veterinarians, etc.) report any of 77 specific diseases and that laboratories report any of 42 specific organisms identified to the local health department. While health care providers are typically concerned with the health of an individual patient, the focus of public health nurses and epidemiologists is on the “big picture” of health in a community.

A single case of a disease may not cause alarm in a physician’s office. However, timely and accurate reporting of communicable disease data allows health department personnel to determine whether this single case may be part of a larger problem in the community. With complete information, health department personnel can check if the disease is related to other cases as part of a cluster or is part of an outbreak (where the number of cases is greater than the number expected during a defined period of time).

#### Disease Detectives

Public health nurses and epidemiologists act as detectives who try to connect pieces of a puzzle in solving disease mysteries. These public health professionals monitor disease information to determine if there are more cases of a particular disease than expected. In addition, they investigate cases of disease to discover clues that may link the infected individuals and uncover the source of their infection. Once the culprit is discovered, these public health professionals provide education to those who are ill and those at risk of becoming ill to help prevent the spread of infection.

#### Benefits

Timely and accurate reporting of communicable disease information thus allows health department personnel to:

- Quickly identify single or multiple cases of disease occurring within a similar location or time
- Identify persons at risk of acquiring or transmitting disease
- Identify care needs and recommend appropriate prevention measures for those affected
- Provide education for future prevention
- Assess the effectiveness of public health disease prevention programs

#### Chronic Disease Surveillance

Chronic diseases cannot be transmitted from person to person. Examples of chronic diseases are heart disease, diabetes, and cancer. Poor health behaviors (lack of physical activity, smoking, poor eating habits, etc.) may increase a person’s risk for chronic disease.

Many of the advances in public health and life expectancy in the United States during the 20th century were a direct result of communicable disease control. Until roughly the 1950s, most Americans died of infectious disease. With these diseases under control and Americans living longer, the major disease burden in the US shifted to chronic diseases. Recently, health issues such as obesity, asthma, and infant mortality have gained a lot of attention in the media and are important issues to address as we strive to achieve a healthier America.

#### Limitations

The nature of chronic diseases presents difficulty when attempting to assess their impact on a community. No formal reporting requirement exists to assist with chronic disease surveillance. Cancer registries exist that allow public health professionals to measure the incidence and prevalence of certain cancers. Beyond that, however, we rely mainly on death certificates that give an indication of causes of death. Although useful, death certificate information is limited in that it is based upon a doctor’s diagnosis, and underlying causes of death are often masked by that which was determined to be the primary cause. Assessing the impact of chronic diseases in a community is thus an inexact science.

#### Behavioral Risk Factor Survey

Because surveillance for chronic disease is difficult, public health professionals rely on collecting information on health behaviors to give an indication of a community's risk for acquiring diseases such as heart disease, diabetes, and cancer. To this end, the Kent County Health Department performs a Behavioral Risk Factor Survey (BRFS) approximately every five years to quantify the presence of particular behaviors in a sample of Kent County residents. This survey collects information on access to health care, smoking, diet, physical activity, sexual behaviors, alcohol use, use of safety belts, and firearm safety. Although the actual presence of disease cannot be quantified through such data collection efforts, risk factors for these diseases can be identified. Once problems are identified, the information collected can be used to direct public health intervention efforts to address the problem at hand.

#### Other Chronic Disease Data

In addition to the BRFS, Kent County personnel monitor data on mortality rates, prenatal care, and lead poisoning to help determine the impact of chronic disease in our society.

Chronic diseases and conditions have been variously defined. A EURO symposium in 1957 gave the following definition:

"An impairment of bodily structure and/or function that necessitates a modification of the patient's normal life, and has persisted over an extended period of time".

Another EURO symposium in 1965 observed:

"Up to now no widely acceptable definition (of acute or chronic patients) has been found. Some authors maintain that an acute illness usually consists of a simple episode of fairly short duration from which the patient returns to normal activity, whereas a chronic illness is one of long duration in which the patient is permanently incapacitated to a more or less marked degree. There is also the view that progress in the technology of resuscitation and haemobiology has blurred the borderline between acute and chronic conditions".

The Commission on Chronic Illness in USA has defined "chronic diseases" as "comprising all impairments or deviations from normal, which have one or more of the following characteristics:

- a. are permanent
- b. leave residual disability
- c. are caused by non-reversible pathological alteration
- d. require special training of the patient for rehabilitation
- e. may be expected to require a long period of supervision, observation or care".

In short, there is no international definition of what duration should be considered long-term, although many consider chronic conditions are generally those that have had a duration of at least 3 months. A practical definition should be established which will suit the particular conditions of the community.

Non-communicable diseases (NCDs) include cardiovascular, renal, nervous and mental diseases, musculo-skeletal conditions such as arthritis and allied diseases, chronic non-specific respiratory diseases (e.g., chronic bronchitis, emphysema, asthma), permanent results of accidents, senility, blindness, cancer, diabetes, obesity and various other metabolic and degenerative diseases and

chronic results of communicable diseases. Disorders of unknown cause and progressive course are often labelled "degenerative".

### The problem

Chronic non communicable diseases are assuming increasing importance among the adult population in both developed and developing countries. Cardiovascular diseases and cancer are at present the leading causes of death in developed countries (e.g., Europe and North America) accounting for 70 to 75 per cent of total deaths. The prevalence of chronic disease is showing an upward trend in most countries, and for several reasons this trend is likely to increase. For one reason, life expectancy is increasing in most countries and a greater number of people are living to older ages and are at greater risk to chronic diseases of various kinds. For another, the life-styles and behavioral patterns of people are changing rapidly, these being favorable to the onset of chronic diseases. Modern medical care is now enabling many with chronic diseases to survive. The impact of chronic diseases on the lives of people is serious when measured in terms of loss of life, disablement, family hardship and poverty and economic loss to the country. Developing countries are now warned to take appropriate steps to avoid the "epidemics" of non-communicable diseases likely to come with socio-economic and health development.

### Non-communicable disease risk factors

Most epidemiologists accept that six key sets of "risk factors" are responsible for a major share of adult non-communicable disease morbidity and premature mortality. These are as follows:

1. Cigarette use and other forms of smoking
2. Alcohol abuse
3. Failure or inability to obtain preventive health services (e.g., for hypertension control, cancer detection, management of diabetes)
4. Life-style changes (e.g., dietary patterns, physical activity)
5. Environmental risk factors, e.g., occupational hazards, air and water pollution, and possession of destructive weapons
6. Stress factors

### Gaps in natural history

There are many gaps in our knowledge about the natural history of chronic diseases. These gaps cause difficulties aetiological investigations and research. These are:

1. Absence of a known agent:

There is much to learn about the causes of chronic disease. Whereas in some chronic diseases the cause is known (e.g., silica in silicosis, asbestos in mesothelioma), for many chronic diseases the causative agent is not known. The absence of a known agent makes both diagnosis and specific prevention difficult.

2. Multifactorial causation:

Most chronic diseases are the result of multiple causes –rarely is there a simple one-to-one cause-effect relationship. In the absence of a known agent, the term "risk factor(s)" is used to describe

certain, factors in a person's background or life-style that (make the likelihood of the chronic condition more probable. Further, chronic diseases appear to result from the cumulative effects of multiple risk factors. These factors may be both environmental and behavioral or constitutional. Epidemiology has contributed massively in the identification of risk factors of chronic diseases. Many more are yet to be identified and evaluated.

### 3. Long latent period:

A further obstacle to our understanding of the natural history of chronic disease is the long latent (or incubation) period between the first exposure to "suspected cause" and the eventual development of disease (e.g., cervical cancer). This makes it difficult to link suspected causes (antecedent events) with outcomes, e.g., the possible relation between oral contraceptives and the occurrence of cervical cancer. In an attempt to overcome this problem, a search has been made for precursor, lesions in, for example, cancer cervix, oral cancer and gastric cancer. But this is not possible in all chronic diseases. However, it has now become increasingly evident that the factors favouring the development of chronic disease are often present early in life, preceding the appearance of chronic disease by many years. Examples include hypertension, diabetes, stroke, etc.

### 4. Indefinite onset:

Most chronic diseases are slow in onset and development, and the distinction between diseased and non-diseased states may be difficult to establish (e.g., diabetes and hypertension). In many chronic diseases (e.g., cancer) the underlying pathological processes are well established long before the disease manifests itself. By the time the patient seeks medical advice, the damage already caused may be irreversible or difficult to treat.

### Integrated approach:

It is now felt that the principles of prevention of CHD can be applied also to other major non-communicable diseases (NCDs) because of common risk factors. A broader concept is emerging, that is, to develop an overall integrated programme for the Prevention and Control of NCDs as part of primary health care systems, simultaneously attacking several risk factors known to be implicated in the development of non-communicable diseases. Such concerted preventive action should reduce not only cardiovascular diseases but also other major NCDs, with an overall improvement in health and length of life.

### Measuring the burden of the disease

The burden of CHD may be estimated in various ways, each illustrating a different aspect of the picture.

(a) Proportional mortality ratio: The simplest measure is the proportional mortality ratio, i.e., the proportion of all deaths currently attributed to it. For example, CHD is held responsible for about 30 per cent of deaths in men and 25 per cent of deaths in women in most western countries.

(b) Loss of life expectancy: CHD cuts short the life expectancy. Calculations have been made for the average gain in life expectation that would follow a complete elimination of all cardio-vascular deaths if other mortality rates remain unchanged. The benefit would range for men from 3.4 years to 9.4 years, and even greater for women.

(c) CHD incidence rate: This is the sum of fatal and non-fatal attack rates. Because of its different manifestations, accurate incidence of CHD rates are difficult to compute. Mortality rates can be used as a crude indicator of incidence.

(d) Age-specific death rates: When analysis is planned to throw light on aetiology, it is essential to study the age-specific rates. Age-specific death rates suggest a true increase in incidence.

(e) Prevalence rate: The prevalence of CHD can be estimated from cross-sectional surveys using ECG for evidence of infarction and history of prolonged chest pain. A useful publication to conduct such surveys is "Cardio-vascular Survey Methods" by Rose and Blackburn.

(j) Case fatality rate: This is defined as the proportion of attacks that are fatal within 28 days of onset. The International Society and Federation of Cardiology has suggested that "sudden deaths" be defined to include deaths "occurring instantly or within an estimated 24 hours of the onset of acute symptoms or signs". Data collected in many industrialized countries indicate that 25-28 per cent of patients who suffer a heart attack die suddenly. In about 55 per cent of all cardiac deaths mortality occurs within the first hour.

(g) Measurement of risk factor levels: These include measurement of levels of cigarette smoking, blood pressure, alcohol consumption and serum cholesterol in the community.

(h) Medical care: Measurement of levels of medical care in the community are also pertinent.

### Epidemicity

"Epidemics" of CHD began at different times in different countries. In United States, epidemics began in the early 1920s; in Britain in the 1930s; in several European countries, still later. And now the developing countries are catching up. For example, in Singapore, the standardized death rate from CHD has more than doubled in the past 20 years, rising from 22 per 100,000 population in 1957 to 50 per 100,000 population in 1979. Similar trends have been noted in some other developing countries, e.g. Malaysia, Mauritius and Sri Lanka.

Countries where the epidemic began earlier are now showing a decline. For example, in United States, where the epidemic began in early 1920s, a steady decline was evident by 1968, and a 25 per cent fall in mortality (not morbidity) by 1980. Substantial declines in mortality have also occurred in Australia, Canada and New Zealand.

Several European countries where the epidemic came later, have registered little or no change in rates (e.g., Hungary, Poland). In Great Britain, the epidemic has not shown any decline.

The decline in CHD mortality in US and other countries has been attributed to changes in life-styles and related risk factors (e.g., diet and diet-dependent serum cholesterol, cigarette use and exercise habits) plus better control of hypertension.

The reasons for the changing trends in CHD are not precisely known. The WHO has recently completed a project known as MONICA "(multinational monitoring of trends and determinants in cardiovascular diseases)" to elucidate this issue. Forty-one centres in 26 countries were participating in this project, which was planned to continue for a 10 year period ending in 1994.

When CHD emerged as the modern epidemic, it was the disease of the higher social classes in the most affluent societies. Fifty years later the situation is changing; there is a strong inverse relation between social class and CHD in developed countries.

To summarize, in many developed countries, CHD still poses the largest public health problem. But even in those showing a decline, CHD is still the most frequent single cause of death among men under 65.

### International variations

CHD is a world-wide disease. Mortality rates vary widely in different parts of the world (Table 1). The highest coronary mortality is seen at present in North Europe and in English-speaking countries (e.g., Scotland, northern Ireland, Finland). On the other hand rates in southern Europe are much lower (e.g. Italy, France), and those in Japan, although a rich industrialized country, are extremely low.

Rose calculates that the "incubation period" of CHD may be 10 years or more. This may explain the currently puzzling position of Japan. The Japanese smoke like chimneys, and have increased their fat intake by 200 per cent in recent years, yet have the lowest incidence of CHD in the industrialized world. If Rose is right, CHD may still be incubating in Japan.

## PREVENTION OF CHD

In the 1960s the issue was whether CHD could be prevented or not. Studies were launched, reported and debated, The accumulated evidence led to a broad consensus of expert opinion that CHD is preventable. This is best expressed in a report of the WHO Expert Committee on the Prevention of CHD, which recommended the following strategies:

### a. Population strategy

(i) prevention-in whole populations

(ii) primordial prevention in whole populations

### b. High risk strategy

### c. Secondary prevention

#### a. Population strategy

CHD is primarily a mass disease. The strategy should therefore be based on mass approach focusing mainly on the control of underlying causes (risk factors) in whole populations, not merely in individuals. This approach is based on the principle that small changes in risk factor levels in total populations can achieve the biggest reduction in mortality. That is, the aim should be to shift the whole risk-factor distribution in the direction of "biological normality". This cannot obviously be done by medical means alone; it requires the mobilization and involvement of the whole community to alter its life-style practices that are associated with CHD,

Specific interventions:

The population strategy centres round the following key areas:

1. Dietary changes: Dietary modification is the preventive strategy in the prevention of CHD. The WHO Expert Committee considered the following dietary changes to be appropriate for high incidence populations:

- reduction of fat intake to 20-30 per cent of total energy intake

- consumption of saturated fats must be limited to less than 10 per cent of total energy intake; some of the reduction in saturated fat may be made up by mono- and poly-unsaturated fats

- a reduction of dietary cholesterol to below 100 mg per 1000 kcal per day

- an increase in complex carbohydrate consumption (i.e., vegetables, fruits, whole grains and legumes)

- avoidance of alcohol consumption; reduction of salt intake to 5 g daily or less

2. Smoking: As far as CHD is concerned, present evidence does not support promotion of the so-called "safer cigarette". The goal should be to achieve a smoke-free society. Some governments (e.g., Norway, US) have declared a smoke-free society by the year 2000. Several countries are progressing towards this goal.

To achieve the goal of a smoke-free society, a comprehensive health programme would be required which includes effective information and education activities, legislative restrictions, fiscal measures and smoking cessation programmes.

3. Blood pressure: It has been estimated that even a small reduction in the average blood pressure of the whole population by a mere 2 or 3 mm Hg would produce a large reduction in the incidence of cardiovascular complications. The goal of the population approach to high blood pressure would thus be to reduce mean population blood pressure levels. This involves a multifactorial approach based on a "prudent diet" (reduced salt intake and avoidance of a high alcohol intake), regular physical activity and weight control. The potential benefits and the safety and low cost of this advice would justify its implementation.

4. Physical activity: Regular physical activity should be a part of normal daily life. It is particularly important to encourage children to take up physical activities that they can continue throughout their lives.

Primordial prevention:

A novel approach to primary prevention of CHD is primordial prevention. It involves preventing the emergence and spread of CHD risk factors and life styles that have not yet appeared or become endemic. This applies to developing countries in particular. These countries should seek to preserve their traditional eating patterns and life-styles associated with low levels of CHD risk factors.

Since the aetiology of CHD is multifactorial the approach to prevention should be multifactorial aimed at controlling or modifying as many risk factors as possible. The aim should be to change the community as a whole, not the individual subjects living in it.

Several well-planned risk factor intervention trials (e.g., the Multiple Risk Factor Intervention Trial (MRFIT) in the US. The Stanford Heart Disease Prevention Programme in California and The North Karelia Project in Finland have demonstrated that primary prevention can achieve substantial reduction in the incidence of coronary heart disease.

b. High risk strategy

(I) Identifying risk: High risk intervention can only start once those at high risk have been identified. By means of simple tests such as blood pressure and serum cholesterol measurement it is possible to identify individuals at special risk. Individuals at special risk also include, those who smoke, those with a strong family history of CHD, diabetes and obesity and young women using oral contraceptives.

(II) Specific advice: Having identified those at high risk, the next step will be to bring them under preventive care and motivate them to take positive action against all the identified risk factors, e.g., an elevated blood pressure should be treated; the patient should be helped to break the smoking



habit permanently - nicotine chewing gum can be tried to wean patients from smoking; serum cholesterol concentration should be reduced in those in whom it is raised, etc.

Several well planned high-risk intervention studies (e.g., Oslo Heart Study, Lipid Research Clinics Study, in US) have shown that it is feasible to reduce the CHD risk factors.

From a methodological point of view, however, high-risk approach suffers from the disadvantage that the intervention (e.g., treatment) may be effective in reducing the disease in a high-risk group, but it may not reduce the disease to the same extent in the general population which consists of symptomatic, asymptomatic, high-risk, low-risk and healthy people. Further, unfortunately, more than half of the CHD cases occur in those who are not apparently at special risk, and this is one limitation of the high-risk strategy. Nevertheless, recognition and treatment of high-risk cases do make an important contribution to prevention.

### c. Secondary prevention

Secondary prevention must be seen as a continuation of primary prevention. It forms an important part of an overall strategy. The aim of secondary prevention is to prevent the recurrence and progression of CHD. Secondary prevention is a rapidly expanding field with much research in progress (e.g., drug trials, coronary surgery, use of pace makers).

The principles governing secondary prevention are the same as those already set out in the above sections, e.g., cessation of smoking, control of hypertension and diabetes, healthy nutrition, exercise promotion, etc. The most promising results to date have come from beta-blockers which appear to reduce the risk of CHD mortality in patients who have already suffered at least one infarct in the order of 25 per cent. None of the preventive measures discussed earlier lose their importance even after the first attack. For example, cessation of smoking is the most effective single means of intervention currently available in the management of patients after a heart attack. The risk of fatal infarction or sudden death is reduced by 20-50 per cent. If the patient does not stop smoking, nothing else is worth doing.

Despite advances in treatment, the mortality of an acute heart attack is still high: among survivors, around 10 per cent in the first year, and 5 per cent yearly thereafter. Delay in reaching hospital is still considerable even in big cities in the West and may be as much as 3.5 hours. About 30 per cent of all deaths occur within 30 minutes of onset. This is one of the reasons why coronary care units have failed to make impact on the total coronary mortality in the community.

Each strategy - population strategy, high risk strategy, secondary prevention - has its advantages and disadvantages, but the population strategy has the greatest potential.