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Aleatory uncertainties
Epistemic uncertainties
Practical examples of aleatory and epistemic uncertainties

# MEDICAL UNCERTAINTIES
# (Aleatory and Epistemic Uncertainties)

The search for truth is relentless and never ending. One discovery leads to several new questions. When homocysteine level was discovered as a cardiac risk factor, questions about its precise role, its relation with genes and diet, problems regarding its control, etc., came up. When these are answered, a new myriad of questions will emerge.

Introspection can provide answers to some questions in moments but can also take years in some situations. A quick method is to collect evidence from whatever source, collate it, analyse it, and come to a conclusion. Many times this evidence is in terms of numbers — number of subjects with and without disease, number of subjects with different levels of cholesterol, number with different signs-symptoms, etc. The purpose of these numbers is to get a handle on underlying uncertainties and help in reaching to an objective decision. Dealing with vitalities of life, medical research requires that these uncertainties be precisely identified, their magnitude properly assessed, and impact on medical decisions minimised.

This section gives details of various kinds of uncertainties and their sources in medical research. For details of methods to control some of these uncertainties and the tools for assessing the magnitude of the uncertainties, particularly the probability, see Medical Biostatistics.

## VARIETIES OF UNCERTAINTIES IN MEDICAL RESEARCH

Uncertainty is an endemic affliction to all human activities. Science too is immersed in uncertainty even though it works and flourishes. Science is distinguished from other knowledge by its reproducibility. A worker on sequencing of genomes is likely to reach nearly the same result as another if they follow scientific principles. However, two philosophers researching on thought process of Socrates may reach to very different conclusions. This should not occur with any science but medicine is especially vulnerable, more so research. Uncertainties in medical research arise from a large variety of sources.

### SOURCES OF UNCERTAINTIES

Most apparent reason for enormous uncertainties in medicine is the profound variation in this setup. The other is limitation of knowledge that both pushes as well as hampers medical research.

## VARIATION AMONG INDIVIDUALS

Major source of variation in medicine is biological differences among individuals. This includes host factors such as genetic make-up, age, gender, birth-order, height/ weight, and blood group. However, the most important contributor, particularly for pathological conditions, is the environment with which biological factors interact in an intricate manner. A brief is as follows.

Significant environmental factors are diet, nutrition, exercise, and addictions such as smoking; behaviour such as sexual promiscuity and mixing driving with drinking; mental attitude, anxiety, and personality traits; stress and strains, social support (love, affection, and prayer) and culture; infections, hygiene, water, and sanitation; education, income, and occupation; roads, traffic, and vehicles; crowding and housing; availability and utilization of health services and health personnel; and climate, pollution, mosquitoes and flies. Health, disease, infirmity, and injury are a by-product of the interactions amongst these factors, and with the host factors. It is nearly impossible to study so many of them together, and this limitation adds to the volume of uncertainty.

Laboratories vary with respect to equipments, appliances, reagents, and methods; and the quality and quantity of technicians. This also contributes to uncertainty. Diagnostic tools are never perfect even in most ideal conditions, and they do give false negative and false positive results in some cases. Observer variation, such as in measurement of blood pressure, is quite common. Physicians would differ in managing a borderline case such as with intra-ocular pressure 22 mmHg. Effectiveness of a therapy depends on the expertise of the medical attendant, on the quality of prescriptions, availability of drugs, laboratory investigation results, compliance of the regimen, etc. All these vary from situation to situation.

## INCOMPLETE KNOWLEDGE

Two types of deficiencies in knowledge are common. First is lack of full information on a patient either because the patient has forgotten, is not able to explain, the records not available, the investigation required such as CT scan is prohibitively expensive, or because of lack of time as in an emergency situation. Thus, the patient management has to start with incomplete information. All these aggravate uncertainty in research as much as in medical practice.

Second important contributor to the spectrum of uncertainty in medicine is the limitation of knowledge. Medical science is incomplete in many respects. Nobody knows yet a definite protocol to treat an AIDS case, how to revert essential hypertension that could obviate dependence on drugs, or how to treat a patient for urinary tract infections when the patient has impaired renal functions. In addition there are limitations of recall. You might know all that is known for a health condition but the ability to recall everything at the time when a patient is confronted is rare. Physicians and surgeons, just as anybody else, have biases, and the memory storage and recall is always selective. Furthermore the expertise of medical professionals is not uniform. Some are good, and the others are not so good.

## DIAGNOSTIC, THERAPEUTIC, AND PROGNOSTIC UNCERTAINTIES

Most uncertainties confronted in health and disease can possibly be categorized into diagnostic, treatment, and prognostic framework (see Box 1 for examples) and some could be called predictive uncertainties not related to prognosis (examples are in Box 2). A prominent set still

remains that does not fit into this conventional framework (see Box 2 again). However almost all uncertainties can be classified into aleatory and epistemic types. This classification is new to medicine but is a big help in management and control uncertainties. These are described below. The following text is in slightly advanced mode and needs an understanding of the process of empirical research. A basic reader can omit the following two sections without losing continuity.

**Box 1: Examples of diagnostic, therapeutic and prognostic uncertainties**

Many examples are given in the text. Others are as follows.

| | | |
|---|---|---|
| Diagnostic uncertainties in | – | exercise stress test for coronary artery disease |
| | – | FNAC, ultrasonography, and mammogram for breast cancer |
| | – | extensive clinical evaluation, multiple sweat chloride test and genotype analysis for cystic fibrosis |
| Therapeutic uncertainty in | – | surgical treatment for asymtomatic gland-confined prostate cancer |
| | – | high-energy photon external beam treatment planning for cancers |
| | – | management of ductal carcinoma in-situ because of possibility of recurrence after conservative surgery |
| | – | early stage of breast cancer |
| Prognostic uncertainties in | – | severe sudden illness |
| | – | early prediction of irreversible brain damage after ischaemic stroke |
| | – | terminally ill patients |

## Box 2: Predictive uncertainties and unclassifiable uncertainties

Medicine is largely a science of prediction—prediction of diagnosis, prediction of outcome of treatment or surgery, prediction of prognosis. But there are many other types of predictions as cited below.

- Gender of a child soon after conception.
- Number of years a person would live after onset of a particular chronic disease.
- Number of AIDS cases likely to come up every year in India for which the country has to prepare for providing care and support.
- The year when leprosy would be eradicated from the world.
- How many people will die by different causes in the year 2025 in any specific country.

There are other uncertainties that are not classifiable into diagnostic, treatment or prognostic framework nor as predictive uncertainties.

- Clinical significance of thromboembolic disease.
- Dynamics of infection, transmission, pathology, and control of schistosomiasis.
- Factors responsible for higher longevity in women.
- How to measure positive health.

## Box 3: Sources of medical uncertainties

ALEATORY UNCERTAINTIES (INHERENT)

- Biological — nonmodifiable (age, gender, heredity or genetic make-up, birth-order, height, etc.).
- Biological — modifiable (anthropological, physiological, biochemical).
- Socio-economic (income, education, and occupation) that can affect personal hygiene, nutrition, and self-esteem.
- Cultural, behavioural and psychological (mental status, family system, faith in prayers, sexual practices, addictions, personality traits, tension-anxiety-stress, etc.).
- Observers, instruments and laboratories—inherent variation in measurements.
- Environmental (climate, dust, mosquitoes, flies, pollution, sanitation, water supply, infection load, quality and quantity of health facilities, family and societal support, communication, traffic, laws and their enforcement, etc.).
- Multifactorial (life-style, hygiene, nutrition, knowledge-attitude-practices, susceptibility, utilisation of health services, etc.; importantly, sampling fluctuations).

EPISTEMIC UNCERTAINTIES (EXTERNAL)

- Universal ignorance about appropriate treatment, cause-effect, etc., for certain ailments, or lack of consensus among experts.
- Nonavailability of data, inadequate knowledge.
- Individual (patient and physician) and societal biases, including biased samples, and suppression of facts.

- Not being able to consider all the factors because they are far too many, or because they are not correctly stipulated.
- Chance that can not be explained, other than inherent variation.
- Nonavailability of appropriate instrument or facility for any particular measurement because it is too expensive or for some other reason, and thus inability to obtain the required information.
- Incompetency, memory lapse, biasedness, carelessness, lack of validity of observers, instruments and laboratories, etc.
- Inadequate design, wrong analysis, or sloppy data interpretation.
- Noncompliance of the regimen or nonresponse.