UNIT 12

REFERENCE VALUES, INDICATORS AND VALIDITY OF DIAGNOSTIC TESTS

Structure

12.1 INTRODUCTION

Several quantitative and qualitative measures are commonly used in medical research, especially for assessing the health of an individual. Measurements are important not only in assessing the level of health, but also in establishing and interpreting the reference values. What do we mean by reference values? How are they established? This is an important aspect which needs understanding, since we will be using the standards/reference/normal values for comparing the results of our data. The present unit focuses on this aspect.

Sometimes we do need to compare the state of health of individuals over a period of time. Such measures are called indicators. In this unit, we will review some of the important mortality and morbidity indicators that measure population health. The last part of the unit will focus on validity of diagnostic tests.

Objectives

After studying this unit, you should be able to:

❖ explain the concept of reference/normal value;

- discuss how the reference values are established and interpreted;
- describe the measure of uncertainty, i.e., probability;
- enumerate the various mortality and morbidity measures; and
- elaborate on the validity of diagnostic tests.

12.2 REFERENCE VALUES: BASIC CONCEPT

Some quantitative measures, normally used in research include anthropometry measures (such as weight for age, height for age etc.), body temperature, respiration rate, hemoglobin values, etc. These measurements are used not only in assessing the nutritional health status, but also in assessing the disease severity. These are also used in establishing and interpreting the reference values of various health parameters. What do we mean by reference or normal values? What is the methodology used to delineate such reference values? We shall discuss these issues here in this section.

What is a reference value?

Normally, in research, we evaluate various parameters/measurements of a subject against a single or a range of reference values. For example, median is regarded as a reference value. We say that the normal body temperature in humans in 98.6^{o}F. We use the NCHS standards and now, more recently, the World Health Organization (WHO) multicentric growth reference study (MGRS) standards for assessing the growth and development of infants and young children around the world. A birth weight of 2.5 kg and above is considered as normal. Similarly, a BMI value between 18.5 to 24.9 is the ideal value for us to remain healthy. Another index to assess growth is percent of median. In India, the classification of children, which is extensively used to group children into various grades of malnutrition is the one proposed by the Indian Academy of Pediatrics. Children with body weight more than 80% of median are considered as normal, a measure below 80% regarded as under nutrition of Grade I; below 70% of Grade II; below 60%, of Grade III; and below 50% of Grade IV.

Having gone through the discussion presented above, you would have got an idea about what a reference or normal value is. Next, let us get to know how these reference values get established. In fact, let us learn about the normal probability distribution.

Normal Probability Distribution

The above discussion indicates that the measurements are evaluated against reference or normal values. Establishment of normal or reference values needs an understanding of the distributional aspects of the measurement. Let us understand this concept. Nutritional requirements, which like many other biological characteristics, vary for different individuals, arising due to inherent differences between individuals. The distribution of requirement for proteins of adults is called 'Gaussian' or 'normal distribution'. Figure 12.1 represent an ideal normal distribution curve.

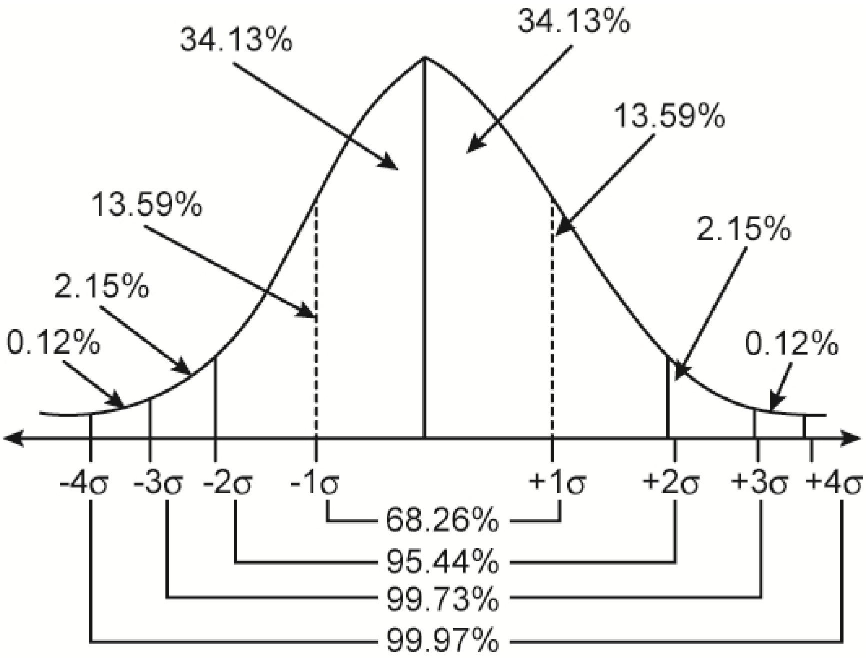

Fig. 12.1: Ideal normal distribution curve

The normal probability curve has the following characteristics:

1) The curve is symmetrical around its vertical axis called ordinate. It implies that the size, shape and slope of the curve on one side of the ordinate are identical to those on its other side.

2) The values of mean, mode and median computed for a distribution following this curve, are always the same.

3) The height of the vertical line called ordinate is maximum at mean and in the unit normal curve, it is equal to 0.3989.

4) The curve is asymptotic. It approaches but does not meet the horizontal axis and extends from minus infinity to plus infinity.

5) The points of inflection of the curve occur at points ±1, standard deviation ($\pm 1\sigma$), above and below the mean. Thus, the curve changes from convex to concave in relation to the horizontal axis at these points.

6) About 68.26 per cent of the total area falls between the limits $M + 1\sigma$ and $M - 1\sigma$; 95.44 per cent of the total area of the curve falls between the limits $M + 2\sigma$ and $M - 2\sigma$ and 99.73 per cent of the total area of the curve falls between $M + 3\sigma$ and $M - 3\sigma$.

Based on the above properties of the normal distribution, the use of ± 2 SD limit as reference is considered. The normal values or reference values are based on measurements of healthy subjects, preferably the healthiest segments of the population. However, it is important to note that while many measurements in healthy subjects follow a Gaussian or normal pattern, all do not. Iron requirements for females, for example, are a highly negatively (left) skewed distribution portraying the likelihood that a given level of usual intake is inadequate to meet the true needs as shown in Figure 12.2. Similarly, distribution can be right-skewed (as in the case of blood lipid in adult male) because the higher levels are more common than lower level.

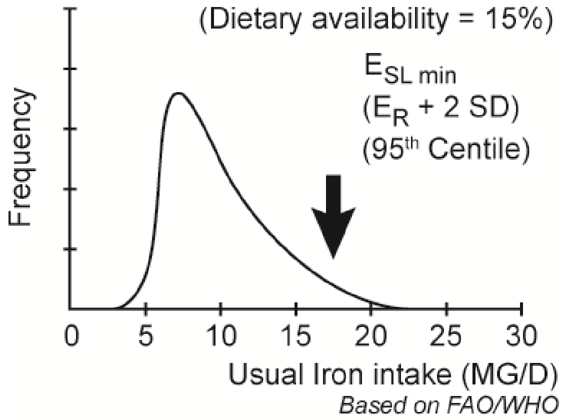

Fig. 12.2: Representative graph showing iron requirement

The use of ± 2 SD limits as reference is not without risk. These limits, as you may have noticed, in any case, exclude those 5% of healthy subjects who have very low or very high values. However, there may be many subjects with disease who may have values well within a normal range. Figure 12.3, illustrates this overlap. This figure also illustrates the wider-dispersion, generally seen among the diseased subjects, compared to the healthy subjects. This overlap gives rise to false positivity and false negativity about which we will discuss in section 12.4. Thus, there is always a risk of misdiagnosis and missed diagnosis in marginal cases. Such risk or uncertainty is measured by probability which is discussed in the next section. Before we end our discussion on reference values, let us also review the interpretation and the comparison of measures with reference values.

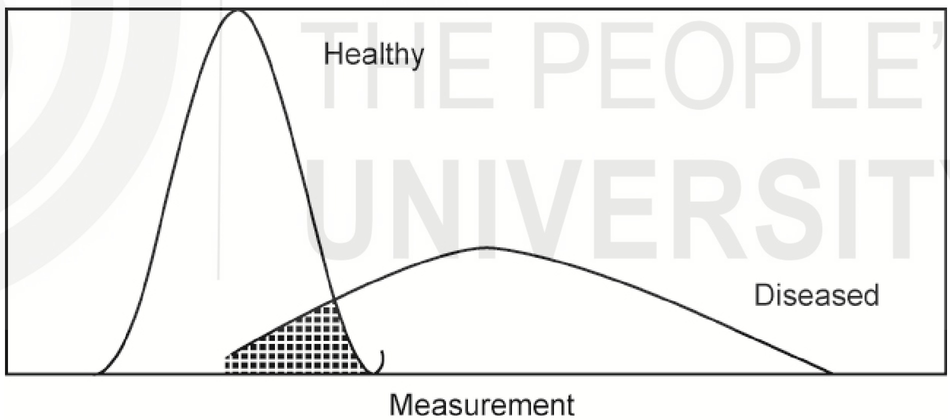

Fig. 12.3: Overlap of values in healthy and diseased subjects

Interpretation and comparison of measures with reference values

Let us understand this concept with the help of an example. The anthropometric measures, for example, we know are assessed by the percentile point achieved by a child relative to the healthy children of that age and gender in the same population. Median is regarded as a reference value, and 3rd and 97th percentiles as the thresholds to indicate abnormally low and abnormally high values.

The interpretation and comparison of anthropometric measurements with reference values is sometimes performed by computing an index called *Z-score,* which is a measure of the distance in standard deviations of a sample from the mean.

Z-score for weight is given by the following formula:

$$Z - \text{score} = \frac{(\text{Weight} - \text{Median})}{\text{SD}}$$

where, Median and SD (standard deviation) are calculated for the reference healthy population of that age or of that height. Z-score below -2 is considered low and below -3 very low.

Z-score, therefore, tells us how a single data point compares to normal data. Z-score represents not only whether a point was above or below average, but how unusual the measurement is.

With this basic understanding, let us next move on to the study of the measure of uncertainty, i.e., probability.

12.3 PROBABILITY: A MEASURE OF UNCERTAINTY

Very often, you might have come across statements such as 'Probability of his/her survival is low". When the first heart transplant was done, the chances of success were rated as 80%. What do these statements indicate? Further, let us consider another example.

Example: You have a coin which has a head and the tail side. After tossing the coin, what is the probability of the coin landing on each side?

Solution: The chances of landing on heads is 1 in 2, or half

The chances of landing on tails are 1 in 2, or half

This example asked us to find some probabilities involving a coin. The probability of each outcome in this example is always the same, i.e., 0.5.

Let us next consider another example of dice.

Example: A single 6-sided dice is rolled. What is the probability of getting each outcome? What is the probability of rolling an even number, or rolling an odd number?

In this example, let us first consider the outcomes and then the solution.

Outcome: The possible outcomes of rolling a dice are 1, 2, 3, 4, 5 and 6.

Solution: The likelihood of number 1 to 6 (outcome) occurring is 1/6

The likelihood of odd numbers (1, 3, 5) occurring is 3/6 = 1/2

The likelihood of even numbers (2, 4, 6) occurring is 3/6 = 1/2

Having gone through the examples presented above, you would have got some idea about the concept of probability. In the light of these examples, let us look at the definitions and few specific examples of probability.

What is probability?

Probability is the measure of the likelihood of an event and is complementary to uncertainty. It can be interpreted as the relative frequency of an outcome in a large number of cases as indicated in the formula given here:

$$\text{Probability (P) of an outcome} = \frac{\text{Number of cases with the desired outcome}}{\text{The number of cases}}$$

Let us consider an example specific from a research view point. Suppose if the statistics of a country suggests that the occurrence of anemia among children under 3 years of age is 7 in 10, the probability of occurrence of that complaint is 7/10 = 0.7. The probability of one or more disease together can also be computed accordingly. Some laws of probability are helpful such as the law of multiplication of probability (for independent events, the joint probability of the two occurring together is easily computed by the product of the individual probability, i.e., {P (A x B) = P (A) x P (B)}, the law of addition (i.e., for mutually exclusive categories P (A + B) = P (A) + P (B).

The probability of an event is generally represented as a real number between 0 and 1, inclusive. An impossible event (such as a male giving birth to a child) has a probability of exactly 0, and a certain event (such as death) has a probability of 1, but the converses are not always true; probability 0 events are not always impossible (i.e., women of 50 years of age conceiving), nor probability 1 events certain. Further, no probability could be negative, nor can it exceed one.

Probabilities are equivalently expressed as odds, which is the ratio of the probability of one event to the probability of all other events. The odds of heads-up, for the tossed/spun coin are (1/2)/(1 - 1/2), which is equal to 1/1. This is expressed as "1 to 1 odds" and often written as "1: 1".

We hope you have got a good insight into the concept of probability and now you should be able to measure uncertainty, linked with your data, using the accepted measure of probability. Next, we shall focus on the indicators used in epidemiological research.

12.4 INDICATORS: MEASURES OF MORTALITY AND MORBIDITY

In our study so far, we focused on the establishment and interpretation of individual based measurements and their reference/normal values. However, in research, we often need to work with a community or a group of people. We may need to compare the state of health/nutrition of a group of people over a period of time in the same community, among people of different biological groups such as of different age, different gender or different race. Such measures are called *indicators.* This term is generally used when the measure is restricted to a specific aspect. There are several indicators of mortality and morbidity that measure health/nutritional status of the community groups. Here, let us review these indicators in greater details. We begin with the indicators of mortality.

12.4.1 Indicators of Mortality

Nutritional/health status can be assessed by mortality rate which is an indirect method of assessment. Let us begin by first understanding the term mortality rate. Mortality rate is defined as the number of deaths in a group of people, usually expressed as deaths per thousand. It is customary to use the term "mortality rate" when the denominator is live births and the term "death rate" when the denominator is population size.

Death is easy to identify in all cases and the date of death is often easily available in records. Thus, the mortality rates/statistics are considered reliable and used world over as indicators for poor health/nutritional status. Indicators used to measure death in a population include crude death rate (CDR), infant mortality rate, child mortality rate, life expectancy at birth, maternal mortality rate, etc. The different indicators that measure mortality in population groups, including children and women are summarized below.

Indicators related to mortality

Indicators based on Foetal Death

1) $\text{Abortion rate} = \dfrac{\text{Abortions}}{\text{Female of reproductive age group}} \times 1000$

2) $\text{Abortion rate} = \dfrac{\text{Abortions}}{\text{Live births}} \times 1000$

3) $\text{Still Birth ratio} = \dfrac{\text{Still birth}}{\text{Live births}} \times 1000$

4) $\text{Still Birth rate} = \dfrac{\text{Still birth}}{\text{Still births} + \text{Live births}} \times 1000$

5) $\text{Perinatal Mortality rate} = \dfrac{(\text{Late foetal}^* + \text{early neonatal}^*)\text{ deaths}}{\text{Late foetal deaths} + \text{Live births}} \times 1000$

*Early Neontal deaths are deaths occurring during first week of life (< 7 days)

Late foetal death includes the foetuses of more than or equal to 28 weeks of gestation. In case where gestation period is not available, a weight of more than or equal to 1000 grams is considered.

6) Perinatal Mortality Ratio =

$$\frac{(\text{Late foetal} + \text{Early neonatal deaths})\text{ weighing} > 1000\,\text{g}}{(\text{Live births})\text{ weighing} \geq 1000\,\text{g}} \times 1000$$

Indicators of Child Mortality

$$\text{Neonatal Mortality Rate (NMR)} = \frac{\text{Neonatal deaths}^*}{\text{Live births}} \times 1000$$

$$\text{Post - neonatal Mortality Rate (NMR)} = \frac{\text{P}ost - neonatal\text{ deaths}^*}{\text{Live births}} \times 1000$$

* Neonatal period is up to 28 days of life (less than 4 weeks) and the post-neonatal period is 28 days to 364 days. These two together form the infant period (less than one year of age)

$$\text{Infant Mortality rate (NMR)} = \frac{\text{Deaths of infants}}{\text{Live births}} \times 1000$$

$$\text{Under - five Mortality rate (U5MR)}^* = \frac{\text{Deaths of children} < 5 \text{ years}}{\text{Live births}} \times 1000$$

*U5MR is also called child mortality rate. Sometimes, mortality in 1-4 years age group is also termed child mortality rate.

Indicator of Maternal Mortality

Maternal Mortality Rate: It is a measure of the risk of death directly related to the pregnancy, once a woman has become pregnant. It is usually measured in terms of maternal deaths per 100,000 life births.

Other Mortality Measures

Crude Death Rate: The number of deaths (irrespective of age) in an area in a year per 1000 population counted at mid-year.

Age Specific Mortality Rate (ASDR): It is a mortality rate limited to a particular age group. The numerator is the number of deaths in that age group while the denominator is the number of persons in that age group in the population. For example, the age specific death rate (ASDR) for the age 1-4 years is the death in age 1-4 years per 1000 children of this age group. Note the ASDR for the age group 0-4 years is different from the U5MR because the denominator represents population of this age group in ASDR, but number of live births in U5MR.

Standard Mortality Ratio (SMR): This is the ratio of the number of deaths observed in a study group to the number that would be expected if the study group had the same specific rates as in a “standard group”. This is multiplied by 100 and expressed in terms of percentage.

$$\text{SMR} = \frac{\text{Observed number of death}}{\text{Expected number of death}} \times 100$$

where, the denominator is based on the age specific rates in a standard population. This can be obtained by multiplying the age-specific population in a sample by the age-specific mortality rates in a standard population. Thus, a form of standardization using predefined ASDRs of a standard population is called standard mortality ratio.

Cause-Specific Mortality Rate: The cause-specific mortality rate is the mortality rate from a specified cause for a population. The numberator is the number of deaths attributed to specific cause. The denominator represents the population size at risk at the midpoint of the time period.

Life Expectancy at Birth: The number of years new-born children would live, if subject to the mortality risks prevailing for the cross-section of pupulation at the time of their birth.

Now you are familiar with the various indicators that measure the mortality in a population group and how to measure them. Next, we shall focus on the morbidity measures.

12.4.2 Indicators of Morbidity

In clinical research, the term morbidity refers to the state of being diseased. It primarily refers to departure from health. *Morbidity rate* is defined as the number of people ill during a time period divided by the number of people in the total population.

Consider the following examples, highlighting the morbidity measures:

Example 1: According to the tenth five-year plan, over the years, there has been a substantial decline in the *prevalence* of leprosy from 57/10,000 in 1981 to 5/10,000 in the year 2000.

Example 2: In India, available data from small-scale studies indicate that the annual *incidence* of sexually transmitted diseases (STD) may be about 5 per cent (40 million new cases every year).

Example 3: During the first 9 months of national surveillance for Eosinophilia Myalgia Syndrome (EMS), the Centers for Disease Control, USA received 1,068 case reports, of which 893 cases were in females and 175 in males. The female-to-male ratio for EMS was 5.1 to 1 (i.e., there were just over 5 female EMS patients for each male EMS patient reported) and the proportion of EMS cases that were males worked out to about one out of every six reported EMS cases.

In the examples presented above, you would have noticed that *proportion, ratio, prevalence* and *incidence* are some measures used to define morbidity. Besides these measures, rate and count are also used sometimes to measure morbidity. Let us explain these measures.

Prevalence

Prevalence refers to the *number of existing cases of disease* or health condition in a population at some designated time, i.e., the extent or presence of a health problem.

$$\text{Prevalence} = \frac{\text{Cases}}{\text{Total population}}$$

Prevalence data provide an indication of the extent of a condition and may have implications to the provision of services needed in a community. It is computed on the basis of existing cases. Prevalence can be computed as:

Point prevalence, i.e., existence of a disease at one point. For example, the NFHS data reports a prevalence of 73% in Indian children less than three years of age. A survey to identify the affected cases generally takes weeks or months, but the count obtained is point prevalence when the inquiry is with regard to the presence or absence of morbidity at the time of contact or a particular reference point. A prevalence rate (per cent, per thousand, or per million persons) can be calculated for specific age, gender, occupation, etc. Prevalence rate estimates the probability of presence of morbidity in a randomly selected person from that group.

Period prevalence, i.e., number of cases that exist during a specified period of time. Note the numerator in period prevalence contains number of cases existing at the beginning plus number of new cases diagnosed during the time period.

Both the above measures of prevalence are proportions and not rates. They are useful in describing health burden of a population; estimate the frequency of an exposure and allocation of resources. Prevalence data are useful for determining the extent of a disease (particularly chronic) in a community. They are not really helpful for studies of disease etiology for which incidence data are better as you would find out next.

Incidence

Example 2 stated above represents the case of use of incidence in research. *Incidence* describes the rate/risk of development of a disease in a group over a certain time period. Incidence is expressed as a rate, and is a much more dynamic measure than prevalence and fundamental in research that pursues the causality of disease. Unlike prevalence, which measures morbidity based on the existing cases, incidence *is the measure of fresh occurrences and is computed on the basis of new cases.* Incidence is considered to measure the risk of getting the disease.

Note that an incidence rate includes three important elements. These include

1) a numerator which includes the number of new cases - only those that have contracted disease since monitoring began are included in the numerator.

2) denominator (population at risk) - excluded should be those who have the disease or those who cannot develop the disease, and

3) specification of time (period during which the cases accrue) - week, month, year or multi-year period. Importantly, we must be able to determine the time of onset.

Besides the incidence measure, an alternative form of incidence rate is useful for short observational periods. This measure is called *attack rate* which is described next.

For diseases such as diarrhea, asthma and pneumonia, the same child can get two or three attacks. In such cases, it is easier to talk in terms of attack rate than incidence, which can be calculated as under:

$$\text{Attack rate} = \frac{\text{New spells during a specified time interval}}{\text{Total population at risk at the midpoint of the same interval}}$$

This term is generally used when the exposure is for a limited period such as during an epidemic.

Before we end our study of incidence, we would like to highlight the interrelationship between *prevalence and incidence.* You would realize that it is easier to find prevalence than incidence. Note that the prevalence of a disease is proportional to the incidence rate (I) multiplied by the duration (D) of the disease, i.e., Prevalence = I x D. Duration of the disease does not affect incidence, but severely affects prevalence. Prevalence tends to accumulate and becomes higher in case the duration is long. Since prevalence depends on the incidence and duration, the relationship can be exploited to find incidence on the basis of prevalence and duration. If there are no intervening factors,

$$\text{Incidence} = \frac{\text{Prevalence}}{\text{Average duration of sickness}}$$

where incidence and duration are in the same time unit.

Besides prevalence and incidence, you may come across measures such as count, rate or ratio, presenting morbidity data. Let us get to know about these measures as well.

Count

Count merely refers to the number of cases of a disease or other health phenomenon. It is not much important in and of itself. It is analogous to case-study. The importance of the number is dependent upon the disease being studied / evaluated.

Rate

Rate is a measure of frequency of occurrence of a phenomenon. Rate is a fraction, like proportion, but different in that the denominator involves a measure of time (unit size) and the numerator consists of the frequency of disease over a specified period of time; viz., two periods of time, beginning and ending.

Thus, the essential components of a rate are (i) a numerator, (ii) a denominator, (iii) specification of a time, and (iv) a multiplier like per cent or per thousand (can be reported in any number of convenient forms; typically per 1,000; 100,000 or 1,000,000 cases). The numerator in a rate is a part of the denominator. For a situation where the numerator is not a part of the denominator, the term ratio is used. We shall learn about ratio next, but here it is important to remember that rate improve one's ability to make comparisons.

Ratio

In Example 3 stated above, you would have noted that the number of EMS cases that were males out of total subjects studied represents a proportion. On the other hand, number of male EMS cases, relative to number of EMS female cases, represents a ratio.

Broadly speaking, therefore, the ratio is one quantity relative to another. It is expressed as a : b or as a/b.

With this, we end our study of the measures of morbidity. We shall next review yet another widely used statistics used to describe a diagnostic test, i.e., sensitivity and specificity.

12.5 MEASURES FOR VALIDITY OF DIAGNOSTIC TESTS

When undertaking research, you would realize that there are many tools used for evaluation and management of health and disease. These tools/tests are seldom perfect. You would very often be confronted with the question "Which test/tool would be most appropriate for my study from the variety of tools available"?

For example, in settings where resources for hematological estimation are not available or hemoglobin estimation is not feasible, recognition of severe anemia by clinical examination (pallor, pica, underweight, etc.) is one of the means of case finding. However, the important aspect to consider here is whether this tool (say recognition of severe anemia by pallor testing) is accurate and will produce correct results in all cases. The ability of a tool or a procedure to correctly perform its assigned function is called validity. Accuracy of a test can be expressed through indicators such as specificity, sensitivity, positive predictive and negative predictive values. These measures are defined and explained herewith.

Sensitivity

The ability of a test to give positive results in true cases of a disease is called *sensitivity.* The sensitivity to the disease is the probability that if the person has the disease, the test will be positive.

Thus, sensitivity is the proportion of true positives of all diseased cases in the population. It is a parameter of the test and calculated as under:

$$\text{Sensitivity} = \frac{\text{Number of true positive (TP)}}{\text{Number of true positive (TP)} + \text{Number of false negative (FN)}}$$

A sensitivity of 100% means that the test recognizes all sick people as such. The larger the number of false negatives, the less the sensitivity.

Sensitivity, however, alone does not tell us how well the test predicts other classes (that is, about the negative cases). The other component of validity of a test is specificity. Let us get to know about this measure next.

Specificity

Specificity is the ability of the test to give negative results in cases not suffering from the disease. It may be calculated as under:

$$\text{Specificity} = \frac{\text{Number of true negative (TN)}}{\text{Number of true negative (TN)} + \text{Number of false positive (FP)}}$$

The specificity is a statistical measure of how well a test correctly identifies the negative cases, or those cases that do not meet the condition under study. For examples, for a medical test to determine if a person has a certain disease, the specificity to the disease is the probability that if the person does not have the disease, the test will be negative. A specificity of 100% means that the test recognizes all the healthy people as healthy. The larger the number of false positives, the lesser is the specificity.

Predictive Value

Predictive values are primarily post-test probability. The diagnostic value of a test is measured by the probability of presence of disease among those who are test positives, and the probability of absence of disease among those who are test negatives. These indicators are called positive predictive value and negative predictive value, respectively. These can be calculated using the following formula:

$$\text{Positive Predictive Value} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

$$\text{Negative Predictive Value} = \frac{TN}{TN + FN}$$

Note as the prevalence of the disease changes, the predictive values are severely affected. This occurs even though the sensitivity and specificity remain constant. As the prevalence increases, the positive predictivity also increases and this increase is more pronounced when the specificity is low. Higher prevalence leads to less negative predictivity, more so when sensitivity is low.

Let us understand the concept of sensitivity, specificity and predictive value with the help of an example.

In a field study (Kapur et al, Indian Pediatr 2002; 36), 545 children were screened for various signs/symptoms (pallor, pica, underweight, diarrhea, fever, worm infestation. respiratory tract infection) and risk factors associated with iron deficiency anemia. Children were also assessed for anemia and iron deficiency using cyanmethaemoglobin estimation method and serum ferritin assessment, respectively as the gold standard. The presence and absence of each of the signs/ symptoms were matched with the Hb levels (anemic/non-anemic) in the subjects and the discordant pairs compared using the chi-square test. Data show that the pallor was significantly associated with anemia. Table 12.1 presents the matched hemoglobin and pallor data for severely anemic children (i.e., Hb < 7.0 g/dl).

Table 12.1: Matched subjects for pallor and hemoglobin (< 7.0 g/dl)

Pallor	**Hemoglobin concentration**		**Total**	
	< 7 g/dl	**≥ 7 g/dl**		
Present (Positive)	20 (True positive)	100 (False Positive)	120 (All with positive test)	Positive Predictive Value = TP/(TP+FP)
Absent (Negative)	21 (False Negative)	383 (True Negative)	404 (All with negative test)	Negative Predictive Value = TN/(FN+TN)
Total	**41**	**483**		

Table 12.2 presents the sensitivity, specificity (converted to percentage by multiplying by 100, using the formula given above) and predictive value parameters for the matched hemoglobin and pallor data.

Table 12.2: Sensitivity, specificity and predictive value of the test of pallor

Hb Cut-off (g/dl)	**Sensitivity (%)**	**Specificity (%)**	**Positive Predictive Value (%)**	**Negative Predictive Value (%)**
< 7.0	48.8	79.3	16.7	94.8

It is evident from the table that the sensitivity and specificity of clinical screening for anemia using conjunctival pallor were 49% [20/20 + 21) x 100] and 79.3% [(383/383 + 100) x 100], respectively, for identifying children who were severely anemic (with Hb < 7.0 g/dl). The positive and negative predictive values are 16.7 [(20/20 + 100) x 100] and 94.8% [(383/383 + 21) x 100], respectively.

Thus, from the example above, you must have got an idea about the measures used to validate tools and how to assess predictivity, using probability.

SAQ

i) Define the following terms:

a) Prevalence; (b) Standard mortality ratio; (c) Reference value; (d) Z-score

ii) State the different characteristics of the normal probability curve.

iii) What do you mean by specificity of a diagnostic test?

12.6 SUMMARY

- Several quantitative and qualitative measures are commonly used in medical research, especially for assessing the health of an individual. Measurements are important not only in assessing the level of health, but also in establishing and interpreting the reference values.
- We evaluate various parameters/measurements of a subject against a single or a range of reference value(s).
- Establishment of normal or reference values needs an understanding of the distributional aspects of the measurement.
- The normal probability curve is symmetrical around its vertical axis called ordinate. It implies that the size, shape and slope of the curve on one side of the ordinate are identical to those on its other side. The values of mean, mode and median, computed for a distribution following this curve, are always the same.
- Probability is the measure of the likelihood of an event and is complementary to uncertainty. It can be interpreted as the relative frequency of an outcome in a large number of cases.
- The probability of an event is generally represented as a real number between 0 and 1, inclusive.
- Mortality rate is defined as the number of deaths in a group of people, usually expressed as deaths per thousand.
- The different indicators used to measure death in a population include crude death rate (CDR), infant mortality rate, child mortality rate, life expectancy at birth, maternal mortality rate, etc.

- Morbidity rate is defined as the number of people ill during a time period divided by the number of people in the total population.
- Prevalence data provides an indication of the extent of a condition and may have implications to the provision of services needed in a community.
- Incidence describes the rate/risk of development of a disease in a group over a certain time period. Incidence is expressed as a rate, and is a much more dynamic measure than prevalence and fundamental in research that pursues the causality of disease.
- Prevalence of a disease is proportional to the incidence rate (I) multiplied by the duration (D) of the disease.
- Rate is a measure of frequency of occurrence of a phenomenon.
- The ability of a test to give positive results in true cases of a disease is called sensitivity. The sensitivity to the disease is the probability that if the person has the disease, the test will be positive.
- Specificity is the ability of the test to give negative results in cases not suffering from the disease. The specificity is a statistical measure of how well a test correctly identifies the negative cases, or those cases that do not meet the condition under study.
- The diagnostic value of a test is measured by the probability of presence of disease among those who are test positives, and the probability of absence of disease among those who are test negatives. These indicators are called positive predictive value and negative predictive values, respectively.

12.7 TERMINAL QUESTIONS

1. What is meant by normal distribution? Briefly describe the concept.
2. Name one index which is commonly used to compare anthropometric measurements with reference value. How is this index computed?
3. Define the terms morbidity and mortality.
4. List one mortality measure, each for assessing the health status of infants, children and maternal nutritional status.
5. What are the two most commonly used morbidity measures in research? What is the relationship between these two measures?
6. Define the following terms:

   i) Sensitivity

   ii) Specificity

   iii) Positive and negative predictive values

12.8 ANSWERS

Self-Assessment Questions

i) Refer to Section 12.2, Subsections 12.4.1 and 12.4.2.

ii) Refer to Section 12.2.

iii) Refer to Section 12.5.

Terminal Questions

1. Refer to Section 12.2.
2. Refer to Section 12.2.
3. Refer to Subsections 12.4.1 and 12.4.2.
4. Refer to Subsection 12.4.1.
5. Refer to Subsection 12.4.2.
6. Refer to Section 12.5.

SUGGESTED READINGS

1. Bogduk N (2022) on understanding the validity of diagnostic tests. Interventional Pain Medicine Vol. 1 Supplement 2, 100127.
2. Hassanzadeh J, Rezaianzadeh A (2012) Assessing the validity of diagnostic tests, Iranian Journal of Medical Sciences 37(1):2.