Clinical statistics: five key statistical concepts for clinicians

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Abstract (J Korean Assoc Oral Maxillofac Surg 2013;39:203-206)

Statistics is the science of data. As the foundation of scientific knowledge, data refers to evidentiary facts from the nature of reality by human action, observation, or experiment. Clinicians should be aware of the conditions of good data to support the validity of clinical modalities in reading scientific articles, one of the resources to revise or update their clinical knowledge and skills. The cause-effect link between clinical modality and outcome is ascertained as pattern statistic. The uniformity of nature guarantees the recurrence of data as the basic scientific evidence. Variation statistics are examined for patterns of recurrence. This provides information on the probability of recurrence of the cause-effect phenomenon. Multiple causal factors of natural phenomenon need a counterproof of absence in terms of the control group. A pattern of relation between a causal factor and an effect becomes recognizable, and thus, should be estimated as relation statistic. The type and meaning of each relation statistic should be well-understood. A study regarding a sample from the population of wide variations require clinicians to be aware of error statistics due to random chance. Incomplete human sense, coarse measurement instrument, and preconceived idea as a hypothesis that tends to bias the research, which gives rise to the necessity of keen critical independent mind with regard to the reported data.

Key words: Pattern, Variation, Relation, Error, Critical mind

[paper submitted 2013. 9. 25 / accepted 2013. 9. 26]

I. Introduction

Electronic digital technology innovates the production and transport of clinical information with unprecedented speed and quantity. We may feel overwhelmed with the massive wealth of clinical information in journals. Statistically trained eyes and minds to see the major points of data and judge the validity of data quickly and accurately are mandatory survival skills in the digital information age. In this article, five key statistical concepts for busy clinicians without formal statistical training are succinctly and clearly reviewed to help them keep up with the times.

II. Variation Statistics

The evolution of human society has been generally accom-

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plished owing to civilization based on science. Knowledge through scientific method was fundamentally different from knowledge from other sources such as authority, superstition, mystery, and personal experiences. In science, any idea (hypothesis) should be crucially tested to verify whether the idea fits the facts. A crucially tested idea becomes acceptable provisional knowledge. As to the status of being provisional, the old knowledge is on the brink of continuous challenge of revision with new facts. Every problem of civilization has been solved successfully because the scientific test confirmed the prediction of phenomenon in reality. This makes science the most powerful tool we have for getting to the truth of things[1]. Thus, the recurrence of the phenomenon is the core difference from knowledge from other sources, called extrapolation or inference. Human beings can expect the outcome of phenomenon with certain probability with knowledge from science. Technology developed from scientific knowledge brings about civilization, which is a production of man-made artificial environments. Civilization always helps human beings overcome the obstacles of harsh natural enviroments. Disease has been one of the infamously fearful, irritating nature, encroaching the quantity and quality of human happiness. Health care professionals intervene in the progress of disease to enhance the quantity and quality of life of patients.

Such professional intervention should be based on rational scientific evidences to verify that there is real benefit and no iatrogenic harm. Empirical evidences from the accumulation of mere personal experiences are not acceptable, since the probability of recurrence of the beneficial outcome could not be quantified. If the beneficial outcome observed by man would not occur again before his eyes, none of the health care professionals and patients would accept any therapeutic intervention. Objective impersonal data providing high probability of occurrence of the favorable outcome in repetition are required for the justification of routine therapeutic intervention. Owing to the specific knowledge of the conditions for the therapeutic outcome, the health care professional is able to master the therapeutics' outcome and to expand the scope of considerable power over the diseases. Nonetheless, powerful recurrent evidences result from rigorous scientific investigation. The two major scientific activities of human beings--observations and experimentations of therapeutic phenomenon under varying conditions of interventions including surgery and medication--have supplied objective, recurrent, predictable data to clinicians. Clinicians who acquire clinical knowledge from journal articles should carefully scrutinize the probability of recurrence of data with the help of variation statistics such as standard deviation.(Table 1) Standard deviation provides information on the possibility of recurrence of mean; the smaller the standard deviation is, the higher the probability of expected recurrence of the same mean in other patients.

III. Counterproof of Absence

Scientific evidence requires not only proof of presence but also counterproof of absence[2]. Proof that a condition always accompanies a phenomenon does not warrant conclusions with certainty that the condition is the immediate cause of such phenomenon. It must still be established that, when this condition is removed, the phenomenon will no longer occur. If we limit ourselves to proof of presence alone, we might fall into error at any moment and believe in the relations of cause and effect when there was nothing but simple coincidence. The human brain is equipped with the ability to sense the presence of immediate change. Unfortunately, the general inability to think about absence is a potent source of error. Thus, co-occurrence (how many people who have bruxism have temporomandibular dysfunction?) and non-co-occurrence (how many people who have bruxism do not have temporomandibular dysfunction, and how many people who do not have bruxism have temporomandibular dysfunction?) and co-absence (how many people who do not have bruxism do not have temporomandibular dysfunction?) occur. All these numerical statistics are necessary to evaluate accurately the likelihood that the two things have a real causal relationship. As long as the phenomenon of causal relationship is real, we can anticipate the same or similar clinical outcome when we apply the knowledge to our clinical practice.

IV. Pattern Statistics

Patterning is the repetition of the same phenomenon in a group[3]. Thus, the distinction of pattern is one of the major contributions of statistics to the community of health care professionals. It has increased the confidence of clinicians in providing clinical intervention to patients expecting a favorable outcome without being afraid of any iatrogenic harm. Observation or experimentation should be performed on a sufficiently large number of human or animal subjects to make sure that a certain same phenomenon occurs on a large number of subjects. The mounting evidence concretizes the therapeutic patterns as more internationally collaborating scientific activities confirms the same phenomenon across gender, age, race, and region. Relations of clinical intervention with positive outcome tend to become a pattern as the number of phenomena accumulates due to the law of large numbers. Therefore, patterning with the repletion of observation of a large number of objects is referred to as pattern statistics. Most clinicians with inadequate statistical concepts tend to focus their attention to representative numerical pattern statistics such as mean only. Pattern statistics should always be

Table 1. Summary of key statistical concepts

Clinical modality	Outcome	No outcome	Pattern statistics	Variation statistics	Relation statistics	Error statistics
Exposure	a	b	$\frac{a}{a+b}$	Standard deviation	$\frac{\text{Proof of presence}}{\text{Counterproof of absence}}$	P-value, confidence interval
No exposure	c	d	$\frac{c}{c+d}$			

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evaluated with variation statistics.

V. Relation Statistics

Once the pattern is ascertained numerically, pattern statistics can be compared to describe the pattern of relation between clinical modality and outcome. Representative statistical instruments comparing the proof and counterproof of connections between the clinical intervention and the clinical outcome are relation statistics, e.g., odds ratio, relative risk ratio, and survival ratio. Clinical statistics are concerned about relation statistics because of the impossibility of knowing the essence of clinical interventions. Instead, we are able to estimate the relations of things. For example, dental clinicians are not aware of the essence of osseointegration of dental implants with human bones. Nonetheless, they know the relations of osseointegration with the longevity of dental implants under the ordinary masticatory function. Thus, health care professionals should be familiar with the correct interpretation of relation statistics. In addition, the comparison of magnitude of relation statistics sheds light on the major definite conditions. Due to limited time and resources, health care professionals and patients should make a choice among the many treatment options[4]. The ascertainment of the most determining factor for the best prognosis obviously assists in the most cost-effective treatment planning.

VI. Control Group

Unlike physical or chemical science, clinical science is where finding the truth of relation is hardest because of the complexity of human phenomenon[5]. Thus, cause-effect links are not always simple or straightforward. First, effects can result from a combination of causes because human beings are creatures inhabiting physical, mental, and social environments[6]. Effects are rarely associated with a single causal factor. In clinical domains, it is very commonplace to see a list of many possible causal factors for the therapeutic effect. Second, both causes and effects can be seen in groups rather than individuals. For example, cigarette smoking causes lung cancer in a certain proportion of people. In other words, causation is not an all-or-nothing matter. Not every subject exposed to a causal factor will necessarily yield the effect. Two statistical devices have been developed: other things being equal control group and multivariate statistical methods. The control group whose conditions are the same as those of the test group except the conditions under observation is required

to single out the definite conditions to produce the phenomenon. Without the control group, it is impossible to attribute any condition to the immediate cause. Thus, a case report without a comparative group cannot provide determinant evidence of cause-effect relation between clinical intervention and therapeutic outcomes. That is why a case report must be regarded as a mere suggestion of further rigorous scientific investigations. Clinicians should not apply what they have read in a case report to their patients immediately. The most famous nearly perfect tool for ensuring comparability is randomization. Matching is another tool for controlling other potential causal factors. All other contributing (confounding) factors are equally represented within both groups. Depending on the type of effect variables such as interval, binary (nominal), and censored, the statistical analysis of multiple causal factors includes multiple statistical models such as linear regression, logistic regression, and Cox hazard regression.

VII. Error Statistics

Statistically-minded clinical scientists think that the task of finding the truth of relation is not that simple. The pattern of strong relations supported by large relation statistics from a sufficiently large number of objects might be due to chance. Wide variations of clinical objects or events arise from the variety of genes, complex inner and outer environments, and diverse past experiences. If you toss a coin with two sides, the correct probability of observing the front side is 50%. In reality, however, such is not warranted. This is because of the intervention of chance. In the same context, a group of study subjects chosen for a clinical study might always come from a group of population with wide variation. By a clinical study including observation or experiment, we have a chance to look at part of a wide variation of phenomenon, but we do not know where the part is placed in the entire population[7]. Statisticians developed the method of calculating the probability of chance intervention into relation statistics, called error statistics. The concept of error in statistics is somewhat different from ordinary terms, which imply mainly human mistakes. The abstract concept of chance is not something clinicians working with concrete subjects are familiar with. Confidence intervals and *P*-value are representative error statistics estimating the probability of chance intervention. *P*-value=0.07, for example, means that the probability of chance intervention into the observed relation is estimated to be as much as 7%. When we set the acceptable cut-off level to 0.05 (in other words, 5% of chance intervention into the observed

phenomenon), we should consider the observed relation statistics to be unacceptable because of the higher probability of chance than expected (*P*-value=0.07). In the same context, when 95% confidence intervals of relation statistics include 1--which means that the relation pattern of clinical intervention with the therapeutic outcome of the test group is equal to that of the control group--we consider the relation statistics to be highly accidental and the relation to be non-replicable in other subjects. In any scientific activity testing a hypothesis (idea), measurement is mandatory. Since human beings' sense and instruments are imperfect, errors in measurement are inevitable. In addition, scientific reasoning with regard to the collected data is prone to error because the preconceived idea (working hypothesis) guiding the research activities is biased toward the investigator's expected outcome.

VIII. Critical Mind

No data could be 100% free from any error. Unfortunately, human mistakes and bias owing to the investigator's subconscious favored hypothesis are impossible to enumerate. The only concern is how much the error contaminates the data. If the level of contamination does not erode the direction or magnitude of the cause-effect link too much, it is acceptable. Note, however, that skepticism on the hypothesis is not desirable because all knowledge is provisionally proven hypothesis, and nobody knows the validity of hypothesis. Only a crucial test, not man, can judge the validity of the hypothesis. We simply judge the validity of evidentiary data in terms of accuracy and recurrence. Criticism on the hidden errors in the evidence and investigating method of any research article is the process of uncovering errors[8]. Investigators should not regard any criticism on their works as an assault on their dignity. Otherwise, too defensive attitude and avoidance of criticism may hinder the progress of science. If a clinical scientist understands that the falsification of hypothesis is a core part of the scientific method, critical comments on any research could be accepted without any mental resistance. In particular, we tend to resist ideas competing with our own automatically. Nothing could be more damaging than abandoning the critical mind and replacing it by too quick acceptance of hypothesis based on weak evidence. These mental attitudes may subconsciously influence a person toward acceptance of claims on plausibility. Hastily jumping to a conclusion to escape from mental pain is natural untrained phenomenon. We should discard opinions that are not based on fact and suspend judgment. Thus, scrutinizing erroneous data thoroughly, discarding opinions that are not based on valid data, and looking for the right explanation for a long time instead of jumping to a conclusion hastily make for the essence of critical and reflective mind for capable clinicians. The critical faculty of a clinician's mind should be developed and trained continuously such that critical attitude becomes an automatic response. By looking at--and looking for--the key concepts of clinical statistics, clinicians can continue the lifelong journey to completion. As Goethe said, "We see only what we know."[8]

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