Experiences in Teaching Biostatistics in the Pharmaceutical Industry and University

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1. " Education " is one of the most essential topics that rise always to people's consideration, regardless of now and then, in all age. In any area of researches and studies, or even when learning various kinds of sciences, the first principle is to learn what a human is. Especially, in the fields of medical science and treatment, we have to know that patients are the most significant of people who participate there. Without knowing this fact, the people are not able to join the process of the medical treatment which consists of the prevention, diagnosis, treatment and prognosis. On the other hand, statistics is known the grammar of the science, compared with mathematics that is the language of the science. However, in statistics, we may often face with events or phenomenon in which a human always lies between. In this sense, it can be said, " Statistics is the science of a human ".

The first author had been involved for over 30 years in the works related with" design "and " analysis "of data in the field of the medical science and treatment, at the section of information analysis in the Japanese pharmaceutical industry. And then, in eight years afterwards, the first author has been engaged in the education and research of statistical science, especially the medical and computational statistics at the Japanese university (Osaka University). In addition, the second author now works as an expert statistician at the section of biostatistics in the global pharmaceutical industry, and is devoting all time to face with the design and analysis of real data in the medical practice.

In this paper, we introduce our limited experiences with the design of data in the observational and experimental studies at the pharmaceutical industry and provide several lessons learned from our experiences. Also, we describe some issues in the global standardization in the clinical evaluation of drugs. Furthermore, we introduce activities of " beginner professor " in the education and research of statistical science at the university, and then provide several lessons learned from our experiences for reference to succeeding people though our experiences are short and limited.

2. A drug must be passed through all hurdles and examinations of the multi-step evaluation process without stagnation so that it is created as a compound, it appears to an actual clinical field as a medicine, and then its effect is demonstrated. The evaluation process of the drug should be necessarily developed, by controlling costs (function) with time and risk as primary indexes, so that the evaluation process is smoothly accomplished in accordance with the principle of utility. In addition, the people who participates the process should always consider the ethics, science and reliability in the methodology and the execution form even as for the

nature of the medicine. That is, the process inevitably forms a lot of aspects, and then it surely requires sincere harmonization and cooperation of phased progress and a lot of participated people. Thus, a lot of problems usually occur in between the phases and cooperation.

When working in the pharmaceutical industry, the first author accomplished various works generated during such a development and evaluation process of drugs. That is, the authors were involved in wide range of works from analogy evaluations such as drug development, manufacturing, chemistry/pharmacology and animal toxicity to clinical evaluations across Phase I, II III and post market. Furthermore, the authors especially accomplished various works generated in the process of the prevention, diagnosis, treatment, and prognosis in medical treatment for the incurable disease, lifestyle disease, psychiatric disease and so on. These works were often consultations that came from the doctors, and if anything, almost of them were exploratory data analysis for searching hypotheses. In addition, the authors had to accomplish the management work in their organization as a leader since the first author became the leader of the organization and then guided their companion or advanced work in cooperation with them as aged.

Then, in order to accomplish works smoothly as organization cooperation by the limited number of people, the philosophy that became one prop or idea that demonstrates readership was necessary.

The concept of " Leaning (Souji), Daily Work (Gongyo), and Study (Gakumon) ", which acquired as " learning character " to the first author during his childhood, was effective there. Referred to author's personal understanding of this concept, " Cleaning " is the standardization, " Daily Work " is the operational work and " Study " is the research and development. Standardization is an indispensable requirement when the organization improves productivities of their work and evaluates their efficiencies. The authors performed their work with concept of standardization when they had to walk one step of their colleagues ahead as a leader. The process of standardization is not a process of mere pressing and " management ". The transition of skills and experiences (lessons learned and wisdom) is included in the process of providing the standard and improving the level of the standard. In a manner of speaking, the standard includes the source (essence) of failure and successful experiences from predecessors. This is a sense of values as a whole where the labor saving lurks there. Then, the followings are the respects that the authors were noting in the flow of dynamic standardization:

- Standardization is indispensable to the work with a high additional value: This lead to the pursuit of the improvement to the quality of work. In other words, it connects with the direction where the load is not put on the pursuit of the amount.
- Efficiency improvement or the automation is planned for the work with an additional value not high: This posture leads to the pursuit of the economy for suppressing the amounts and costs.
- It can be said that the process of standardization is a process of " awareness " and the practice. It is the process of actualizing the lessons learned and wisdom where the person in charge of the work shows consideration to the process following afterwards, or it shows the achievement of sympathy of the person in charge in the former process.

3. The obligation or work as a professor at the university includes lectures to faculty and postgraduate students, seminar and composition guidance of master and doctor theses, attendance and correspondence of various kinds of internal committees, responses to consultation works, activities at academic society and so on. However, unlike works at the company, almost of such professor's works should be accomplished on their own terms. Therefore, figuratively

speaking, this seems to be like an owner of small and medium-sized enterprise. But immediately execution is not acceptable, not like an owner of small and medium-sized enterprise.

The first author provides lectures on medical and computational statistics for the first and second graders of Departments of Medicine and Human Science. As a statistical textbook, Brown & Hollander (1977) is used for the former and Yang & Robinson (1986) for the latter. Of course, these textbooks are Japanese translated versions and both translated textbook are the work by author's colleagues. At the graduate school, the first author provide lectures on the multivariate analysis without any textbooks, but by using his original Power-Point slides. In compliance with various kinds of demands of the advanced information times, main subjects of master and doctor theses are the data adaptive approaches in statistical data analysis, data investigation methods, statistical diagnostic methods, statistical graphics, and computer intensive methods.

We choose the field of medical science and treatment as statistical practices, and then pursue various statistical issues in clinical evaluation process of drugs. Though the steadfast clinical evaluation processes, which consist of chain of experimental studies, are considered a standard in the medical science, we examine the methodology from the viewpoint that flexibly tempers with the prerequisites for the exploratory research and the confirmation research. Especially, without biasing to the experimental study we pursue the flow of data→ information → knowledge → wisdom from the aspects of the observational study. Then, we funnel our energy into the studies of method for annexation and separation of data, method and outcome in the process of information analysis and its verification method.

When we guide the postgraduate, similarly as worked in the pharmaceutical industry, the idea of " custom of cleaning, daily works, and learning or study " is the basis. At the university, the cleaning (standardization) means " succession and development of culture and literary property ", the daily works includes " personality development " generated from doing routine works or urgent works at the time, and the learning or study corresponds to " research and development ". Mysteriously, cleaning of mind is always neglected at the university. We think that the negligence of this cleaning has destroyed human's moral fiber.

4. There are only three prescriptions in the times with conformational change as statistician can prepare. These include thinking, observation and trials (experiments). Though all these prescriptions seem to be elusive on the face of things, their concreteness is increased if the adjective of " Statistical " is added to these. By the way, " Three principles of the thinking " can be interpreted more plainly with the posture of statistical approach. That is, these are (i) to see only the essence of changing events and matters (think about the noise by removing), (ii) to think about matters on the time axis (long-term aspect), (process intensive approach) and (iii) to consider matters from various viewpoints as much as possible (multivariate thinking approach). Especially, if the adversity refrains from " solitude ", and then provides chances to increase individual ability, the recent atmosphere like a valley between times may be considered the best time for thinking.

The feature of the observation is to see in an untouched appearance, without disarranging the state of the object as a polite fiction, to obtain objective information. Thus, the content of the observation consists of the considerable information-gathering ability, vision that sees through the depths (dark), comparison with the past, tendency clutches by forecast in the future, and accurate judgment power that identifies detail.

The experiment is a trial in a regulated frame that sees how the object behaves when a certain condition is given, with appealing positively to the object, even if the target is natural or human. Therefore, in the experiment, the hypothesis is first of all early, and, then, the experiment has a certain nature of verification. Even if either prescription of the observation or the experiment is adopted, there is the process of the search or the verification of the hypothesis

and the statistical idea (method) becomes indispensable.

5. Ultimately, the personal magnetism is brewed with two elements of the polish of oneself, and making own customer. For the people who intends common sciences (technology) such as statistical science, corresponding to the above two elements, it is inevitably requested to walk in the process of the self-actualization self-concluded, or to promote the interpersonal relationship ability for the expansion and the deep plowing of own cheerleaders. We would recommend the latter standpoint. From the comparison of the research posture in foreign countries with Japan, we are aware of the weakness of the collaborated research situation in Japan. In foreign countries, researchers systematically inquire into the various kinds of subjects by collaborated researches, while it depends greatly on an individual ability in Japan.

It seems that the match of " sharpened bamboo strategy " and " army corps " is settled before it fights. In statistical science, the practice is emphasized. Moreover, any originality doesn't arise in the place where the practice is not effective. Hereafter, we would to enrich the exchange with own cheerleaders on the ring of practice. In other words, this is the practice of collaborated creation and Buddhist saint work.

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RÉSUMÉ

Dans ce papier, nous introduisons nos expériences limitées avec le dessin de données dans les études d'observation et expérimentales à l'industrie pharmaceutique et fournissons des plusieurs lecons apprises de nos expériences. Aussi, nous décrivons des questions dans la standardisation globale dans l'évaluation clinique de drogues. En outre, nous introduisons des activités de. professeur du débutant. dans l'éducation et recherche de science statistique à l'université, et alors fournit des plusieurs lecons apprises pourtant de nos expériences pour référence aux gens suivants nos expériences sont courtes et limitées.