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The use and misuse of statistical methodologies in pharmacology research

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ABSTRACT

Descriptive, exploratory, and inferential statistics are necessary components of hypothesis-driven biomedical research. Despite the ubiquitous need for these tools, the emphasis on statistical methods in pharmacology has become dominated by inferential methods often chosen more by the availability of user-friendly software than by any understanding of the data set or the critical assumptions of the statistical tests. Such frank misuse of statistical methodology and the quest to reach the mystical $\alpha < 0.05$ criteria has hampered research via the publication of incorrect analysis driven by rudimentary statistical training. Perhaps more critically, a poor understanding of statistical tools limits the conclusions that may be drawn from a study by divorcing the investigator from their own data. The net result is a decrease in quality and confidence in research findings, fueling recent controversies over the reproducibility of high profile findings and effects that appear to diminish over time. The recent development of "omics" approaches leading to the production of massive higher dimensional data sets has amplified these issues making it clear that new approaches are needed to appropriately and effectively mine this type of data. Unfortunately, statistical education in the field has not kept pace. This commentary provides a foundation for an intuitive understanding of statistics that fosters an exploratory approach and an appreciation for the assumptions of various statistical tests that hopefully will increase the correct use of statistics, the application of exploratory data analysis, and the use of statistical study design, with the goal of increasing reproducibility and confidence in the literature.

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1. Introduction

The discipline of statistics provides a logical and mathematical framework for the collection, organization, analysis, interpretation, and presentation of experimental data. It is used to analyze experimental outcomes and determine the likelihood that an outcome in a sample population is predictive of the population from which the sample was derived, e.g. to establish the efficacy and safety of a new chemical entity (NCE) in a sample human test population that will allow its broader use in a general population.

There has been growing concern that much of what is published in both the preclinical and clinical literature is misleading, resulting in the creation of a "house of cards" that undermines the core values of the biomedical research enterprise through key findings that cannot be replicated [1,2]. While there are multiple deficiencies that may underlie these shortfalls, the current diminution in the understanding and appropriate use of statistical methodologies can only lead to additional problems. When used with appropriate insight and practical experience, statistics is the *sine qua non* of biomedical research. However, with well-meaning albeit misguided biomedical researchers driving toward the goal of statistical significance, often analyzing inappropriately derived data sets and switching between statistical tests until they get the expected "right" result, it is not surprising that there is a loss of faith in the literature.

Perhaps the greatest hurdle that must be overcome in restoring confidence in research findings is the misunderstanding of what statistics is. To some researchers [3], statistics is believed to be an ephemeral science and the rejection of the appropriate use of statistical design and analysis is defended with quotes like "There are three kinds of lies: lies, damned lies, and statistics" (attributed to both Benjamin Disraeli and Mark Twain). To others, statistics is the right tool for the wrong job being applied when convenient to support a favored theory. For these researchers, "statistics are like a bikini. What they reveal is suggestive, but what they conceal is vital" (attributed to Aaron Levenstein [4]). Rather than an ephemeral science or a convenient multi-tool, statistics is a practical science, encompassing not only data analysis but also the actual design of the experiments used to generate that data.

2. Background

The basic concept of the *scientific method*, a theoretical framework for conducting scientific inquiry, can be found as early as 400 BC in Greek and Chinese texts. In practice, the scientific method involves an iterative testing and modification of hypothesis in order to extract knowledge (Fig. 1). Hypotheses are generated based on previous investigation or knowledge of the subject under investigation, experiments are designed to test this hypothesis, and the results are interpreted and used to modify the original hypothesis generating a new hypothesis for further testing. Within the context of the scientific method, the experimental design process and the interpretation of results are the domain of statistics. *A statistic* is a quantity calculated from a set of data. For example the mean of a set of numbers is a statistic. Statistics (not to be confused with the plural of statistic) is a broad term that encompasses all quantitative aspects of data collection, interpretation, and presentation. The appropriate use of statistics is essential to insure the best methods are used to collect data in an

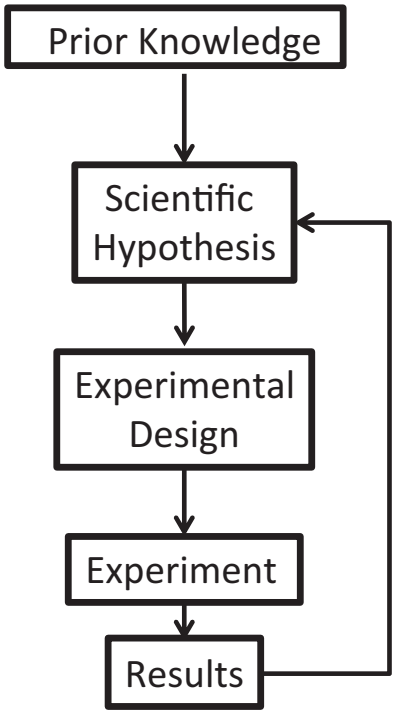

Fig. 1. Flow chart representing the primary steps in the iterative process known as the scientific method.

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