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The Miracle of Biostatistics in Medical Research

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Abstract

Statistical theory and statistical methods have been provided significant results in all scientific disciplines. Today, **Biostatistical methods are being miracle solutions for the complex problems of medical and clinical research**.

Statistics is not mathematics; neither is probability. They have been distinguished probability from statistics. Probability is math; statistics is not. Probability is deductive; statistics is inductive.

According to the Editorial report entitle is to "Looking Back on the Millennium in Medicine" published in New England Journal of Medicine (NEJM); **The application of statistics to medicine as one of the eleven most important medical developments during the last millennium.**

In 1984, the American Association for the Advancement of Science polled leading U.S. scientists asked which were the most important scientific, technological and medical discoveries since 1900?. Statistics (chi-square test) has been taken at 22 th order in the list of " **The 23 most significant scientific contributions to our life in the 20th Century".**

The chronological of statistical development have been started with observation. Statistics is the science of nature, therefore it is considered to be the nature of science.

Statistics accepted as social science in 18 century. Sociologist Adolphe Quatelet_(1796-1874) who has developed Body Mass Index is an establisher of statistics. Adolphe Quetelet was a Belgian social statistician and a forerunner in demonstrating the importance of statistics to social science. In this way Quetelet was a pioneer in developing a whole new
methodology to be used in the social sciences. He felt that using statistics to gather social knowledge was the solution for the betterment of society. The statistics Quetelet gathered have great historical significance.

In the medical field, complex problems are waiting for the solution. This solution will be realized by using powerful statistical methods. **If it needs to specify few methods for 21 th century; the most ones are Recevier Operating Curve Analysis, Logistic Regression, Kaplan–Meier survival curve, Cox proportional hazards regression model, methods for statistical validation** etc.. using the right method, interpret the outcomes correctly will be realize by a study a team with specialist of Biostatistics.

Key words: Biostatistics, ROC, Logistic Regression, Development of Biostatistics, Miracle of Biostatistics, Medical Research

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Introduction

Biostatistics science continues to be the biggest miracle of medical research. The reason for this is that; continue to improve providing the best evidence methods for medical researchers. Researchers expect to use new evidence methods to analyse the complex problems of hypothesis, because they need to trust their own new clinical data more than present research.

I would like to remind the quotation of Karl Pearson here (1857- 1936); "Statistics is the grammar of science (1892)"

Statistical theory and statistical methods have been provided significant results in all scientific disciplines. Today, Biostatistical methods are being miracle solutions for the complex problems of medical and clinical research.

According to the Editorial report titled "Looking Back on the Millennium in Medicine" published in New England Journal of Medicine (NEJM); The application of statistics to medicine as one of the eleven most important medical developments during the last millennium. The presentation "obviously, many more could have been selected. They presented them not in order of importance, but in rough chronologic order according to the first noteworthy step taken in a given area (1).

The results are as follows;

1. Elucidation of Human Anatomy and Physiology
2. Discovery of cells and Their Substructures
3. Elucidation of the Chemistry of Life
4. **Application of Statistics to Medicine**
5. Development of Anesthesia
6. Discovery of the Relation of Microbes to Disease
7. Elucidation of Inheritance and Genetics
8. Knowledge of the Immune System
9. Development of Body Imaging
10. Discovery of Antimicrobial Agents
11. Development of Molecular Pharmacotherapy

The natural starting point for a history of biostatistical thought in the past millennium is the work of Leonardo Fibonacci (c. 1170– after 1240), an Italian mathematician of the middle Ages. By introducing Indian and Arabic mathematics and numbering to Europe in 1202, he freed Western thought from the limitations of the Roman-numeral system (1).

In 1984, the American Association for the Advancement of Science polled leading U.S. scientists and asked which were the most important scientific, technological and medical discoveries since 1900?. The top 23 contributions to our lives are listed, according to importance, in Table 1 (2).

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Table 1. The 23 most significant scientific contributions to our life in the 20th Century

Order of Importance	Discovery
1	antibiotics
2	double helix (DNA and RNA)
3	computers
4	oral contraceptives
5	nuclear (atomic) fission
6	power controlled flight
7	Einstein's theory of relativity
8	solid state electronics (transistors)
9	television
10	Hubble's "big bang" theory
11	quantum mechanics
12	drugs for mental illness
13	plastic
14	networks such as the internet
15	blood types
16	plant breeding
17	lasers
18	plate tectonics
19	the vacuum tube
20	pesticides
21	the Taung skull
22	statistics (chi-square test)
23	the IQ test

Source:
Adapted from: Hacking, 1984; Barnard, 1992

The statistics has been taken in 22 th place at the arrangement of "the 23 most significant scientific contributions to our life in the 20th Century". This important result is not bestowed on every science branch.

The cronolojical of statistical development have been started with observation. Statistics is the science of nature, therefore it is considered to be the nature of science.

Stigler, S.M. presented the five most consequential ideas in the history of statistics (3).

Idea 1: The Combination of Observation
The mean
1635 Henry Gellibrand - used by
1722 Roger Cotes - weighted
1755 Thomas Simpson - proved better
Linear models - Misc & Least Squares
1750 Tobias Mayer
1780s Pierre Simon Laplace
1805, 1809 Legendre, Gauss (LS)

Idea #2: The Root N Rule
Accuracy = 1/St.Deviation $\propto\sqrt{N}$

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Gives a rate for accumulation of information
1713, 1716 Jacob and Nicholas Bernoulli
1730 Abraham De Moivre – binomial
1810, 1812 Laplace - general (CLT)
1879 C. S. Peirce - economy of research

Idea #3: Tests and Likelihood
1248 London Mint, Trial of the Pyx
1710 John Arbuthnot: 1 chance in 2^{82}
1735 Daniel Bernoulli: planetary orbital planes
1922 R. A. Fisher: Likelihood
1933 J. Neyman and E. S. Pearson theory of testing

Idea #4: Statistics by Intercomparison
The internal measurement of variability
1875 Francis Galton - percentiles
1885 Francis Edgeworth – variance components
1908 W. S. Gosset - t-test
1918-1925 R. A. Fisher - ANOVA and design

Idea #5: Regression Phenomena, Correlation, Multivariate Analysis, and Modern Bayesian Analysis
Idea #5: Regression, …
1877-1889 Francis Galton – phenomenon, paradox
1933 Horace Secrist (1970 A. O. Hirschman)
Idea #5: Regression, correlation,…
1893 Francis Edgeworth – multinormal
1895 Karl Pearson - math of correlation
1922-1936 R. A. Fisher – distribution theory etc

Idea #5 (ctd.): … and Bayes
1764 Thomas Bayes
1772-74 Laplace
1877-1889 Francis Galton

Idea #5 (ctd.): … and Bayes
1880s, 1890s Edgeworth, K. Pearson
1930s Harold Jeffreys
1950s Jimmie Savage, Dennis Lindley,…

Statistics accepted as social science in 18 century. Sociologist Adolphe Quatelet_(1796-1874) who has developed Body mass index is an establisher of statistics. Adolphe Quetelet was a Belgian social statistician and a forerunner in demonstrating the importance of statistics to social science. In this way Quetelet was a pioneer in developing a whole new methodology to be used in the social sciences. He felt that using statistics to gather social knowledge was the solution for the betterment of society. The statistics Quetelet gathered have great historical significance (4).

Statistics is not math; neither is probability. They have been distinguished probability from statistics. Probability is math; statistics is not. Probability is deductive; statistics is inductive (5).

Is statistics a science, a technology, or an art? Statistics is not a subject like the basic disciplines of mathematics, physics, chemistry or biology. Each of these disciplines has a subject matter of its own and problems of its own which are solved by using the knowledge of the subject. There is nothing like a statistical problem which statistics purports to solve. Statistics is used to solve problems in other disciplines and appropriate methodology is developed for any given situation (6).

The following Exhibit 1 from a paper by Box (1980) shows how most of the important concepts in statistics were motivated by practical problem (7).

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Exhibit 1. Practical Problems Motivating General Statistical Cocepts (George Box (7))

Practical Problem	Investigator	Derived General Concept
Analysis of Asteroid Data. How far is it from Berlin to Potsdam?	Gauss	Least squares
Are planetary orbits randomly distributed	Daniel Bernoulli	Hypothesis testing
What is the population of France?	Laplace	Ratio estimators
How to handle small samples of brewery data	Gosset	t-test
Improving agricultural practice by using field trials	Fisher	Design of experiments
Do potato varieties and fertilizers interact?	Fisher	Analysis of variance
Accounting for strange eyeles in U.K. wheat prices	Yule	Parametric time series models
Economic inspection (of ammunition)	Wald Barnard	Sequential tests
Need to perform large numbers of statistical tests in pharmaceutical industry before computers were available	Wilcoxon	Nonparametric tests

Statistics is science in the sense that it has an identity of its own with a large repertoire of techniques derived from some basic principles. **Statistics is a technology** in the sense that statistical methodology can be built to any operating system to maintain a desired level and stability of performance, as in quality control programs in industrial production. Statistical quality control is described as one of the great technological inventions og the 20th century. Fisherian framework provided the basis for the development of theoretical statistics during the first half of the 20th century as shown in Exhibit 2. (7).

Exhibit 2. Basic Concepts of Statistical Inference

Author	*Subject*	*Year of Introduction*
Karl Pearson	Chi-square goodness-of-fit	1900
W.S. Gosset	t-test	1908
R.A. Fisher	Exact sampling distributions	1915
	Principles of estimation	1922
	Analysis of variance	1923
	Design of experiments	1926
W. Shewhart	Control charts	1931
J. Neyman & E.S. Pearson	Testing of hypotheses	1933
	Confidence intervals	1938
E.J.G. Pitman	Nonparametric tests	1937
P.C. Mahalanobis & M.Hansen	Sample Surveys	1944
A.Wald	Sequential sampling	1947
	Decision theory	1950

Statistical analysis features in the majority of papers published in health care journals. Most health care practitioners will need a basic understanding of statistical principles, but not necessarily full details of statistical techniques. Medical statistics can contribute to good research by improving the design of studies as well as suggesting the optimum analysis of the results. Medical statisticians should be consulted early in the planning of a study. They can contribute in a variety of ways at all stages and not just at the fi nal analysis of the data once the data have been collected. The use of statistical methods pervades the medical literature. In a survey of original articles published in three UK journals of general practice; *British Medical Journal* (*General Practice Section*), *British Journal of General Practice* and *Family Practice*; over a 1-year period, it has been found that 66% used some form of statistical analysis. It appears, therefore, that the majority of papers published in these journals require some statistical knowledge for a complete understanding. Statistics is not only a discipline in its own right but it is also a fundamental tool for investigation in all biological and medical science. As such, any serious investigator in these fields must have a grasp of the basic principles. With modern computer facilities there is little need for familiarity with the technical details of statistical calculations. However, a health care Professional should understand when such calculations are valid, when they are not and how they should be interpreted (8).

In the medical field, complex problems are waiting for the solution. This solution will be realized by using a powerful statistical methods. If it needs to specify few methods for 21 th century; the most ones are Recevier Operating Curve Analysis, Logistic Regression, Kaplan–Meier survival curve, Cox proportional hazards regression model, methods for statistical validation etc.. using the right method, interpret the outcomes correctly will be realize by a study team with specialist of Biostatistics.

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