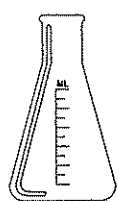


Biopharmaceutical Section



American Statistical Association

Biopharmaceutical Report

Volume 1, No. 2

Summer 1992

Chair: *Camilla Brooks, Ph.D.*

Editor: *Avital Cnaan, Ph.D.*

Teaching Statistics for Understanding and Practical Use

Stephen J. Ruberg
Marion Merrill-Dow, Inc.

Introduction

The reason I have taken an interest in statistical education is two-fold: 1) I work with the products of the educational system, fellow statisticians as well as laboratory scientists and other health care professionals who are, to varying degrees, exposed to statistical methods; 2) I have always been interested in the educational process and have enjoyed part-time teaching jobs at the high school and university level. As a statistician working in industry, I see tremendous variation in understanding of what statistics is all about. I am interested in seeing the educational system improve since it would make my job easier in communicating scientific and statistical concepts.

It seems that many people are deeply afraid of statistics. In fact, many of us know the situation in which we identify ourselves as statisticians in public (and not many of us are willing to do that very often), and the response from other individuals is, "Statistics was my worst subject!" or "All those formulas!" In many instances, we are viewed as mathematical freaks. Thus, when we try to collaborate with other professionals, there is a certain amount of paranoia from them about us doing something with their data that they do not understand. Many of us have recognized the need to improve quantitative literacy in this regard.

What to do about statistical education depends greatly on the particular audience of interest. Many distinct issues must be addressed for majors versus non-majors and undergraduate education versus graduate education. My major emphasis will be on the first course in statistics since that is our best chance at reaching many of the people who need to deal with quantitative information. The people with whom I consult most frequently come out of such courses, and I wish they had a deeper understanding of the statistical method (note the singular form, like the scientific method) rather than the general confusion about which formulas are most appropriate for a particular data set. Furthermore, this first course also may be our only chance to capture the interest of young students with quantitative skills and attract them to the statistical profession. Therefore, the first course in statistics should be radically different than what is presently being done in many textbooks and university curricula, and should focus largely on the major concepts that are relevant to statistical thinking. Finally, I will touch on some aspects of additional courses and more advanced statistical education, but this article is not about mathematical statistics.

I have used a phrase before to describe my feelings about the importance of statistics in our scientific/technological society. It is: **As mathematics is the language of science, statistics is the logic of science** (Ruberg 1990). What I mean is that we are discovering more and more that the world is probabilistic rather than deterministic. As such, we are driven to collecting data that can be subject to different interpretations, and statistics is the means by which these interpretations can be evaluated. Thus, statistics is about logic

Contents

FEATURED ARTICLE

"Teaching Statistics for Understanding and Practical Use"	RUBERG	1
Discussion	SCHEAFFER	5
Discussion	ROMBERG	7
Discussion	HOGG	9
Discussion	GNANADESIKAN	11
Discussion	FREE	12
Discussion	BRADSTREET	12
Rejoinder	RUBERG	14

BIOPHARMACEUTICAL SECTION NEWS

Letter from the Editor	5
Reactions to "Ethics and Clinical Trials"	6
Personal News	6
Minutes—Section Business Meeting, August 1991	8
Software Review—StatXact	10

CONFERENCE REPORTS

Applied Statistics Conference, December 1991	7
Section-sponsored Sessions at ENAR, March 1992	15
Training Course in Non-Clinical Statistics, March 1992	16
Training Course for New Clinical Statisticians, March 1992	17
Merck-Temple Conference on Research Topics in Pharmaceutical Statistics, May 1992	17

UPCOMING EVENTS

ASA Biopharmaceutical Program, August 1992	18
Biopharmaceutical Roundtable Luncheons, August 1992	18
Applied Statistics Conference, December 1992	18
1992 Biopharmaceutical Section Executive Committee	19

and the very underpinnings of the scientific method—how to deal with empirical facts and draw logical conclusions. Statistics, in a sense, is more than a science: it is the very heart of science, the very threads of logic that hold the fabric of science together. This is difficult to teach, since many who have developed logical constructs in their mind tend to do so from a mathematical viewpoint. My own experience has been that a solid foundation in mathematics does not necessarily guarantee the insights and abilities necessary to be successful in statistical thinking.

I should conclude this introduction by stating that I do not mean to be denunciatory about the state of statistical education. I am sure that the Statistical Education Section of ASA, the National Council of Teachers of Mathematics (NCTM), and many other organizations have guidelines for what should be taught in introductory statistics. Their efforts are undoubtedly improving the education system and the textbooks used to teach statistics, especially introductory statistics, as well as stimulating new/experimental approaches to teaching statistics. I will confess that I have not reviewed such materials in preparing this essay, so my comments may be in agreement or in conflict with various aspects of these carefully developed guidelines. However, some of my thoughts are in agreement with recent authors (Watts 1991; Radke-Sharpe 1991; Hogg 1991) on the topic of statistical education and I hope my comments stimulate further thinking.

The First Course

I originally deliberated on what would constitute a good introductory course in statistics for undergraduate students who are not majoring in mathematics or statistics. As that course took shape in my mind, I realized that such a course would be applicable for high school students who have an interest in mathematics or science in general, undergraduate majors in mathematics and statistics, and graduate students who are not majors in mathematics or statistics. I would like to propose a different approach than what I see in many introductory statistics texts. The list of topics is as follows: probability, randomness, variability, estimation, hypothesis testing and statistical significance, experimental design, examples and counter-examples, surveys and observational data. While some of these topics are covered in standard texts, the conceptual approach could be much different. Of course, descriptive statistics, statistical graphics, and exploratory data analysis techniques should be introduced. Some of these topics are covered traditionally, although some newer techniques in graphics and EDA could be incorporated.

Probability. Often we teach combinations and permutations, calculating binomial probabilities, perhaps hypergeometric probabilities, and the like. However, I do not find many people coming away with a notion about what is likely and unlikely to occur. They do not seem to have a notion of coincidence versus causation. The links between birth defects and drug usage, sudden infant death syndrome and vaccines, and many other instances can be cited whereby many people in the public are fooled by coincidence. In his book *Innumeracy*, John Allen Paulos used the term "innumerates" for those who are unable to understand or deal with quantitative information. An inadequate understanding of probability, and therefore the probabilistic world in which we live, plays a large role in innumeracy.

In addition, many people do not understand problems of multiplicity. If a set of data or a collection of facts are examined in a number of different ways, in various subgroups, and with various transformations, it is quite likely that a spurious relationship will emerge. Too often innumerates take these spurious relationships as causal relationships. Computer simulations can be used to illustrate the occurrence of false positive findings.

The concept of Type I and Type II errors is also related to this discussion. In many courses the types of errors may be described

mathematically or probabilistically, but there is a need to put more emphasis on how to interpret such errors and how they might arise from our methods of analyzing data. This would also help students understand risk/benefit considerations. In many ways, our society is risk averse, when there needs to be an understanding of balance between risks and benefits (Type I and Type II errors). We all know the phrase, "There's no free lunch." If one type of error is decreased, the other will be increased.

Randomness. The American Heritage Dictionary gives the following definition: "Random: having no specific pattern or objective, haphazard. Without definite method or purpose." There are many examples of randomness in our society—from things as trivial as the lottery to as complicated as Wall Street stock prices. Many people try to impose logical explanations for what are completely random sequences of observations. A good example of this is those peddlers who write books on how to beat the lottery system. In fact, in the *Cincinnati Enquirer* there was a letter from a person who claimed, "Although the numbers are generated completely at random, certain patterns begin to emerge." We know how ludicrous this is, but it is the view of many individuals in our society who falsely seek to impose order on random observations.

How do we teach randomness in our introductory courses? One can open many introductory texts and find a definition, perhaps couched in terms of a random variable. "Given a sample space, S , a random variable is a rule (function) that assigns a numerical value to each outcome in S ." Most likely, many students do not readily understand what that means or how that is related to randomness. It might be much more important to teach the concept of randomization in introductory courses, i.e., the random assignment of treatments to experimental units and how important this is in removing bias and creating comparable treatment groups for evaluation. This fundamental and simple concept is not readily apparent to many students who have completed an introductory course in statistics.

Variability. We are surrounded by tremendous biological and physical variability, and the concept of variability is readily apparent to many individuals. However, its impact on our logical choices (inference or decision making) is not readily apparent in general. Outcomes of experiments, surveys or virtually any measurement/data collection process will be different from day to day or person to person or clinic to clinic, and therefore *observed* outcomes may not represent the true state of nature. Of course, this is closely tied to probability, randomness, and inference (testing and estimation), and allows one to introduce the concept of a population. There are a variety of exercises and computer simulations that can be performed where the "truth" is known, and the variation of the observed results from repeated "experiments" can be compared to the truth. This leads nicely into the use of simulation in introductory classes and the need for computers.

Hypothesis Testing. Teaching randomization would lead nicely into randomization tests, which I have found in my consulting experience to be quite understandable by scientists. Furthermore, there are very few assumptions we need to make applying such tests, and it eliminates confusion about sampling distributions, t , χ^2 , and F distributions, that arise from normal theory. Randomization tests convey the statistical method (note singular form) better, and the resulting p -values are much easier to interpret. Generating the randomization distribution via computer is relatively easy to do and it would give students hands-on experience with such concepts. It might even be extended into the use of bootstrap methods, which is quite similar and easily implemented on a computer, as is the randomization test. Simon and Bruce (1991) have a nice approach in this regard.

I am often struck by the simplicity of Pearson's chi-squared goodness-of-fit test developed in 1900, which simply compares what is observed in a set of data with what is expected under

certain model assumptions. This is a fundamental concept in statistics, and much of statistics is devoted to comparing observed and expected results. This leads naturally to the logic of statistical inference and its direct connection to the scientific method, a connection that should be explicitly taught. I once explained to a toxicologist that hypothesis testing was like proof by contradiction, but there is a slight difference. In the mathematical world, if we come up with a statement that is false, we know with certainty that our original assumptions or equations are not true. Statistics is no different on this score except that our final conclusion is a p-value—a probability, if you will, that the null hypothesis is true. This brief and simple lesson went a long way in teaching the toxicologist what was going on with the statistical analysis of some of his data.

Of course, we must teach our students the difference between statistical significance and practical significance. Francis Y. Edgeworth said in his Newmarch Lectures given in 1895, "For example, in the case of some recent experiments in so-called physical research the returns prove conclusively that some agency other than chance has been at work. But the calculus [of probability] is silent about the nature of that agency. Whether it is more likely to be some form of illusion, or a less familiar cause, must be decided by common sense." Many explanations and debates have been waged over this lack of understanding of statistical significance versus practical significance.

Estimation. There are many examples in the book *Innumeracy* that emphasize the need for students to actually do some of their own estimation. Some examples are: estimate the number of hairs on a person's head; estimate the number of bricks in a building; estimate the size of a cube that would be necessary to hold all the humans that are presently in the world. This would help students focus on uncertainty in their estimates, what assumptions were made, and what methods were used to arrive at their estimates. Students could learn about data collection, which is rarely discussed in introductory statistics classes, and how it is equally important to data analysis. Such projects are simple to assign and many be very powerful in conveying what many lectures cannot convey.

Experimental Design. An important issue is experimental design versus analysis of variance. Experimental design is a very difficult concept to teach because experimental design is a creative process. Merely teaching the statistical analysis of designed experiments will not impart to the student the creative nature of the experimental design process. I am sure that many of you have had the experience of dealing with someone who insists on doing experiments, controlling one variable at a time. I am equally sure many of you have had similar experiences relating to a statement made to me on one occasion by a Ph.D. pharmacologist: "What does statistics have to do with experimental design anyway?". Although teaching students how to design complicated experiments is unrealistic, students should have some appreciation of how statistics is intimately involved with the experimental design process. Perhaps some simple 2^k factorial experiments could be explained and other examples presented in a very general way. Again, randomization would play an important role here.

Examples. Real-life examples and counter-examples could be very useful in such a course and I would refer again to the book *Innumeracy*. In the introductory course much is to be said for the philosophy of "learn by doing." Many of you are probably familiar with the well worn Chinese proverb that says, "I hear and I forget. I see and I remember. I do and I understand." We should also model statistics as a science much like other laboratory sciences. There should be statistical science labs that include computers for data processing, plotting, simulation, and the like. There is the need for statistics projects such as answering the following questions: What is the quickest route to school or to work? Is it true that one is more likely to hit home runs in Fenway Park than in any other Major League Baseball park? Is Pepsi really the preferred cola?

These can be very complicated questions and students should be encouraged to investigate them to their fullest, as their interests dictate.

Surveys and Observational Data. With respect to observational data (i.e., environmental data or epidemiologic data) collected over many years in uncontrolled conditions, it is very important for students to understand its fundamental difference with data from controlled, randomized, blinded experiments. To help emphasize this, relevant examples in the social sciences and the medical professions would be very useful. In a similar way, some review of surveys and sample survey methodologies is important. Much of what we see in the media is focused on public opinion for various political issues, gauges of consumer confidence in the economy and the like. However, since I have virtually no experience in such methodologies and applications, I will leave comments to others as to how to best involve these concepts early in statistical education without overwhelming students with formulas and technical details.

The Second Course

If students would successfully complete a first course containing those concepts mentioned above, I would consider the course a major success in that we would have reached many in the general population and perhaps achieved some level of understanding about "statistical thinking."

The second course could be focused more on statistical methods (note the plural form) much like what is taught in introductory courses today. In such a course, there could be greater focus on more parametric models, starting with the binomial and normal distributions, as has been done traditionally. This, of course, would be followed by further discussion of probabilities and area under the curve for normal densities and the resulting sampling distributions— t , χ^2 , F . The concept of probability being an area under the curve and the concept of normally distributed data leading to a variety of sampling distributions, are not easy to learn even for the mathematically literate. If these concepts were introduced after a more fundamental understanding of what statistics is all about, perhaps greater success could be achieved in maintaining students' interest and understanding, even if they do not major in mathematics or statistics. Some statistical packages for analyzing data could be introduced, since this could be most useful for people who may need to practice some elementary statistical methods in the future. Some simple, straightforward, PC packages are available for non-majors. For majors, SAS or BMDP could be included.

In this second course, more simulation experiments could be incorporated as part of the "labs." These simulations would assess concepts like power and outcomes of statistical tests when assumptions are violated, such as normality or equal variances. Hands-on experimentation, via simulation, is more likely to produce a better understanding of how this variety of methods can be useful or misleading depending on the situation. Simulations may also help emphasize that results from small experiments or studies can be speculative or limited in their scope.

After the Second Course

For those students who have the interest and the tenacity to continue learning about the science of statistics, more detailed courses, much like we already have on many college campuses, can be taught. These specialty courses would consist of more technical details involving regression, nonparametrics, sampling methodologies, categorical data analysis, and other topics. Of course, these courses could be taught at a variety of technical levels depending on whether students were undergraduate majors or graduate students in statistics. There are many good textbooks that cover these topics and can provide the student with a sound foundation in many statistical methodologies.

I would like to comment a little further on graduate education in statistics. I admit that I am speaking out of my realm of experience and, therefore, my opinions may not carry much weight. I have not worked in the university on a full-time basis so as to have a deep or thorough understanding of the wide variety of pressures and challenges that face academicians. However, I will go out on a bit of a limb and make some suggestions in order to create a lively discussion about these issues.

Every graduate program in statistics ought to include some analysis of real data, both observational and experimental. Furthermore, this analysis and evaluation should be accompanied by interpretation and presentation to fellow students or members on the faculty or to the department as a whole. A lot of what statistics is all about has to do with inference—inference from real data, playing with numbers to reach practical conclusions and real decisions. Fred Mosteller wrote a cogent essay in *The American Statistician* (1988) entitled, "Broadening the Scope of Statistics and Statistical Education." In that article, Mosteller emphasizes that dissertations in statistics should incorporate some investigation of the practical implications of the theoretical statistical findings. Hopefully, such an activity would keep statisticians in touch with what (I believe) statistical science is all about. Ruberg and Louv (1991) have discussed how statisticians can play a strategic role in scientific investigations, and Chatfield (1991) states:

Statistical journals tend to concentrate on developing the methodology of ever-more complicated techniques, which, while important, needs to be complemented by an ability to recognize *when* and *how* to implement such techniques, and to know *why* things are done and what the results mean. Thus, general strategy, which should include the avoidance of trouble, is at least as important as knowing the details of the specific techniques.

In commenting on Chatfield's paper, Mallows and Pregibon state, "Our journals and textbooks are filled with an excessive amount of material on the techniques of data analysis. This energy should be applied to the process of data analysis." If such activities are not done and such perspectives not incorporated, we might as well hand out Ph.D.s in mathematics, because that is how I view some of the research. It is merely doing mathematical proofs and derivations using statistical functions.

I must confess that I am sometimes humored (maybe humored in order to disguise my frustrations) when I see a presentation done on a general theory using "some underlying continuous distribution function F ." After listening for a while and struggling with what the speaker is doing, how he/she is doing it, and why he/she is doing it, I become refreshed with the presentation when I hear the speaker say, "Let me give an example." My enthusiasm turns to disappointment when the example consists of converting capital X 's (random variables) to lower case x 's (observed values), or that the example consists of letting F be some particular distribution, such as a Pearson Type III Distribution with some unknown parameters. I was hoping that the example would have something to do with real life and real data.

I do not mean to say that mathematical statistics is not important. It is a vital foundation on which we can continue to expand our knowledge and develop our methodologies for the ever-increasing complexities of science, technology and society itself. I just mean to say that everyone with an advanced degree in statistics should have some piece of their education devoted to a real problem or two and be forced to think about the analysis, interpretation, conclusions, and even the next step for further application or scientific research. In the pharmaceutical industry and in the areas of biomedical research in general, we certainly need more students with practical experience in solving real world problems, and then accurately communicating the results to clients.

Finale

My premise for this article has been that we as statisticians often jump too far ahead too fast in teaching students about statistics, especially in the first course. Too often, we inundate the student with confusing terminology, a variety of mathematical formulas to use in different situations, and lists of reference tables and prescriptions for decisions rules. We should focus on the statistical reasoning process, not the techniques and calculations. As I said earlier, we, as a profession, should not expect students to take one course in statistics and be able to apply statistical methods to the many types of data to which these students may be exposed in their academic and professional careers. We do not expect students to take one semester of calculus and then to begin designing electronic components and building bridges and highways systems. Clayton's and Nordheim's Commentary agrees with Chatfield (1991) by concluding, "...it is important that such advice [about statistical pitfalls] be regularly incorporated into the introductory and methods courses that are offered to students from other fields who will be the investigators of tomorrow. In particular, these courses should incorporate real world complexity and provide students with the insights to help them avoid the potential statistical pitfalls..." I would say that this advice is equally appropriate for our own mathematics and statistics majors and should be reinforced throughout the curriculum.

Detailed methodologies should be saved for a second course in statistics and beyond. The first course should be much more conceptual and include many elements that we statisticians consider intriguing and fun about our discipline. When asked what it is mathematicians do, one of my graduate mathematics professors simply responded, "We discover what is true." In using statistics we have a very similar goal—only we explore what is *likely* to be true. This is the fun and intrigue of statistics and also its challenge. There is very little in life that is certain; through the appropriate use of statistics we can address challenging problems and issues that impact the well-being of all members of society by moving from uncertainty, to experimentation and data collection, to analysis and to what is *likely* to be best for all of us. This is the fun and intrigue I find in statistics, and that is what I wish we could convey to students early in their statistical education. I hope that many people may understand and appreciate who we are and what we do. I hope that some of the more mathematically or quantitatively inclined students will join our ranks and will create a pipeline of qualified statisticians for the future. This is why the first course in statistics is so critical. As the saying goes: "One never gets a second chance to make a first impression."

References

- Chatfield, C. (1991) Avoiding statistical pitfalls. *Statistical Science*, 6:240-286 (With Comments and Rejoinder).
- Hogg, R. V. (1991) Statistical education: Improvements are badly needed. *The American Statistician*, 45:342-343.
- Mosteller, F. (1988) Broadening the scope of statistics and statistical education. *The American Statistician*, 42:93-99.
- Paulos, J. A. (1988) *Innumeracy*, Hill and Wang, New York.
- Radke-Sharpe, N. (1991) Writing as a component of statistical education. *The American Statistician*, 45:292-293.
- Ruberg, S. J. and Louv, W. C. (1991) The statistician as strategist. *Proceedings of the Statistical Education Section of the American Statistical Association*, 8-15.
- Ruberg, S. J. (1990) The statistical method: The logic of science. *Proceedings of the Statistical Education Section of the American Statistical Association*, 206-211.
- Simon, J. L. and Bruce, P. (1991) Resampling: A tool for everyday statistical work. *Chance*, 4:22-32.
- Watts, D. G. (1991) Why is introductory statistics difficult to learn? And What Can We Do to Make it Easier? *The American Statistician*, 45:290-291.

Discussion

Themes for the First Course and Ideas of Pattern, Association, and Model

Richard L. Scheaffer

University of Florida

Dr. Ruberg makes yet another strong plea for improvement in the teaching of statistics because quantitative reasoning is so important to the sciences. I agree and, in fact, would go one step further to suggest that quantitative reasoning skills are essential for anyone who desires to be either gainfully employed or an informed citizen in the near future. Since I also agree that the first course in statistics is critical, I will confine most of my comments to that course.

Many would agree with the list of topics presented for coverage in the first statistics course, a list that is not far different from the contents of some of the more enlightened of the modern textbooks. Many would also agree that concept development is more important than formula retention or computation. The problem comes when one attempts to tie these topics together in a single, coherent course that gives students an introduction to statistical thinking in a way that can be seen as relevant to their lives. As I will attempt to point out below, even we statisticians can get a little confused on what we are trying to present to students, so it is not too surprising that the students also get confused. I will first comment on the topics proposed in the paper and then close with a summary of my views of the introductory statistics course.

Probability is certainly a key concept for statistical reasoning, but neither an axiomatic approach to the subject nor a formal definition of random variable need be part of an introductory course in statistics. (The topic should not come first either, but I assume that the list does not necessarily imply order.) As Dr. Ruberg points out, what is important is the understanding of the notion of likely versus unlikely, and this can come about through experience in exploring probability by conducting simulations and carefully observing natural phenomena in our world. The fraction of heads does, indeed, "head" toward $1/2$; the .300 hitter is unusual but even he does not get a hit every game. Probabilities for combined events and conditional probability are the real terrors here. These ideas must be approached gently, perhaps through the use of two-way tables of real or simulated data.

An exploratory approach to probability is intimately connected to the notion of randomness, so I do not see these as distinct topics. Random numbers tend to be used as the standard and basic building block for simulation, sampling and experimental design, but how do we describe or check for randomness among a set of digits? We commonly look at a histogram of values produced to observe its PATTERN. What happens when we simulate the performance, say, of a simple queue? We generate many possible outcomes and look at the PATTERN. How do we illustrate sampling distributions for statistics? We randomly sample and then look at the PATTERN produced by the results—the same patterns produced over and over again in different situations. A key to statistical thinking is that randomness generates a predictable pattern. This is a VERY difficult idea for a student to grasp, but lots of hands-on work with simulations seems to help. I disagree with the American Heritage Dictionary; randomness produces pattern and is not haphazard. It is a very cleverly crafted way of producing those patterns that are essential for statistical reasoning. Haphazard collections of data will yield little in the way of useful results.

As the author implies, variability is one of the fundamental (perhaps THE fundamental) concepts of statistics. Students must understand that it is always present (in "varying" amounts) but that one can often measure it and still make intelligent decisions in

spite of it. It is important, in my opinion, to separate variability into appropriate categories, such as variability among the objects being measured (students are of different heights), measurement error (two students measuring the height of a third student will produce slightly different measurements), and sampling error (the average height of students from this class will differ from that of the class in the next room). Which of these can be measured, which can be controlled and which can be reduced by the sampling design gets to the heart of what statistics is all about as a practical tool. Simulation is certainly a good method for beginning to understand variability.

There is a danger, however, in concentrating too much on a fixed population with a known "truth." This is not the way statistics is used in practice and the examples quickly become artificial. In fact, statistical studies mostly involve dynamic populations that are changing while the study is in progress. This leads to the notion of analytic versus enumerative studies, which should be discussed somewhere in an introductory course.

With regard to hypothesis testing, simulation and a data-analytic approach to statistical analyses lead quite naturally to randomization tests and then on to bootstrapping. These topics, which are conceptually simpler than classical testing procedures, should make their way into the introductory courses. (However, I would also downplay hypothesis testing considerably.) More informative procedures such as odds ratios, measures based on concordant and discordant pairs, and graphic displays (P-P and Q-Q plots, for example) should take over some of the time and energy devoted to classical tests like the chi-squared goodness-of-fit test. The p-value is so widely used that it cannot be ignored, but it must be handled with care. (Is the p-value "the probability ... that the null hypothesis is true"?)

Letter from the Editor

Dear Section Members:

I hope you will enjoy the second issue of the *Biopharmaceutical Report*. Many thanks to Dr. Ruberg for writing the lead article on teaching statistics and to the discussants for valuable input and additional insights and information. We are reminded daily of various deep and wide problems in education, and just about everybody has an opinion or personal experience. I would like to encourage Section members to read Steve's paper and the discussion, and if they feel they have something to add to the discussion, or strongly disagree, by all means, write!

On another note, I would like to thank Alison Stern-Dunyak for her competent and cheerful help in putting the *Biopharmaceutical Report* together. Alison does the entire layout and has given many useful suggestions and information which greatly improved the *Report*. The *Report* now also has an associate editor, Thomas Bradstreet from Merck. Tom adds enthusiasm and ability to this endeavor, and has already helped me greatly in producing this issue. Finally, thanks to Chris Gennings, our new publications officer, for her help.

If you are willing to review a new book, or have an interesting consulting problem, please let us know. If somebody joined your group, or received a promotion, or won an award, allow us to share the good news with Section members.

Avital Cnaan

Editor

Responses to "Ethics and Clinical Trials: Some Neglected Issues" by Marvin Zelen

Dr. Zelen presented his paper at a meeting of the Boston Chapter of the ASA. The following are some comments from that meeting, summarized by Louise Ryan.

Dr. Zelen stressed the importance of careful post-marketing surveillance. He said that under the usual 5% acceptable rate for false positives and a false negative rate of 10%, one would expect a ratio of about 2/3 of true positives to all positives. Ellen Hertzmark (Tufts) asked how often it happened where the second and third trials refuted the findings of the first. Jerry Dallal (Tufts) argued that one could view confirmatory trials as an opportunity to provide an otherwise unavailable treatment. Dr. Zelen argued that although this is often the case, trials are often conducted with drugs that are readily available for other diseases. Nick Lange and Katherine Monte pointed out that patients are often confused about the details of a clinical trial. Richard Goldstein argued that confirmatory trials are somehow not a problem when trials are being conducted concurrently.

Another issue discussed was whether there was a "bounty" trial where money is at issue versus a non-bounty trial where research funding and prestige is implicitly involved. Richard Goldstein said on the topic of ethical omniscience, that it was often useful to have an external evaluation.

To the Editor, *Biopharmaceutical Report*:

I enjoyed reading the excellent article by Dr. Zelen and the discussions by others on ethics in clinical trials which appeared in the first issue. There is one issue which I think has an ethical component (Peace, *Proceedings of the ASA, Sesquicentennial Invited Paper Sessions*, 1989), which neither Dr. Zelen nor the discussants mentioned. This has to do with what the informed consent section of a protocol should say about aspects of sample size determination. Some have used the phrase (Art Johnson may have been the first) "Efficacy Imperative" in association with sample size determination. What this means is that it is imperative that the sample size be determined on the basis of large power to address the research question (efficacy) in pivotal proof of efficacy trials. Sample size determination may carry with it an "Ethical Imperative" as well. In my view, it is unethical to fail to inform a potential participant in a clinical trial about the power the trial has to answer the research question. Of course, this presumes that the question has been formulated and the potential participant has also been so informed. Admittedly, this will be difficult to explain to some potential participants, and there is danger in misleading if not explained well. However, were I a potential participant in a trial, I would surely inquire about the sample size and power. I would not want to participate in a trial with low power, since I would know (almost surely) at the outset that the research question would not be answered.

Karl E. Peace, Ph.D.

*President, Biopharmaceutical Research Consultants, Inc. 4600 Stein Road, Suite B
Ann Arbor, MI 48105*

Estimation tends to be used in two different senses, and both are critically important to the introductory course in statistics. One is the exploratory sense in which a student is simply trying to gain some intuition about numbers (number sense, if you will), as in sensing whether the number of hairs on a person's head is closer to 2,000, 200,000 or 2,000,000. The other is the more familiar (to statisticians, at least) use as a formal inferential procedure. It might be good for statistics instructors to treat the former more formally and the latter less formally. The idea of a confidence interval can be taught without getting hung up on degrees of freedom, normality assumptions, and t-tables.

Experimental design is an essential topic for the introductory course, but so is sample survey design. Along with census and observational study, they comprise the ways we get data into the system in the first place. Comparisons among these four (Where, why, and how are they used?) should be made, while emphasizing notions of bias and confounding as well as the role of randomization.

Examples involving real data and projects of interest to the STUDENTS should be an integral part of any introductory statistics course. Most experts agree that hands-on experience is essential to the learning process. The problem comes in trying to find those examples that will, in fact, interest students and any instructor would be wise to call upon his or her students for suggestions.

After many years of thinking about how to teach introductory statistics (and still not being overly successful at it), I have come to think of the course as covering four main themes: exploratory analyses, planning considerations, probability, and confirmatory analyses. Woven into these four themes are the ideas of pattern, association, and model. Exploratory analysis begins with looking for patterns, and departures from patterns, in a single set of data and then goes on to look for possible associations between two or more sets of data. After suitable exploration, questions emerge which can be answered only after a carefully planned study is executed. From a well-posed question and a carefully designed plan for producing data, a model can be formulated for the way in which the measurements might behave. Probability is the tool for anticipating what the data might look like under the model at hand so that decisions (confirmations) can be made as to its credibility.

Dr. Ruberg's suggestions as to the content of the introductory course cover the concepts that are essential to this outline, and I wish him (and others) well in pushing the ideas expressed in this paper. They might take heart in the fact that ideas such as actively involving students in the learning process and making full use of modern technology are recommendations strongly supported by the National Research Council for all of undergraduate mathematics instruction, as stated in *Moving Beyond Myths: Revitalizing Undergraduate Mathematics* (National Academy Press, 1991). With common goals promulgated from many fronts (including the industry covered by this publication) progress will be made!

Personal News

Professor Myron Chang from the University of Florida joined Merck on May 1, 1992, as the first Stanley S. Schor Visiting Scholar. The purpose of this new program is to foster relationships and collaboration between industry and academic statisticians.

Discussion

Statistics at College and High School Level—Some Ideas from the National Council of Teachers of Mathematics

Thomas A. Romberg

Sears Roebuck Foundation—Bascom Professor in Education, University of Wisconsin—Madison

I enjoyed reading Dr. Steven Ruberg's paper. As a mathematics educator, I am concerned about the blasé attitude of many university instructors regarding the quality of collegiate courses in mathematics and statistics. It is refreshing to read a paper by a statistician that challenges the way current introductory courses are typically taught. I agree with the author's assertion that "the first course in statistics should be radically different than what is presently being done in many textbooks and university curricula." In particular, I applaud his concern for the "need to improve quantitative literacy" rather than teach a collection of meaningless formulas. I can only hope that a number of university instructors read and reflect on Dr. Ruberg's treatise. And, I fervently hope that mathematics teachers in the nation's schools also become apprised of this message. In this regard, there are four other comments I want to make.

First, Dr. Ruberg appears to be unfamiliar with the recent curricular recommendations about statistics (e.g., the "Statistics Standards" in NCTM's *Curriculum and Evaluation Standards for School Mathematics*, 1989), or new text materials for high schools on statistics (e.g., the *Quantitative Literacy* materials produced by the American Statistical Association, Landwehr, Swift, & Watkins, 1987), or even the recent reports from professional organizations on the need to change collegiate courses and instruction (e.g., *A Call for Change* by the Mathematical Association of America, 1991; or *Moving Beyond Myths* by the National Research Council of the National Academy of Sciences, 1991). Nevertheless, his recommendations are consistent with the reform vision of those documents. Furthermore, since he is a practicing statistician who consults with individuals whose only statistical experience is in initial university courses, his argument provides experiential validity to the call for radical change in both the "what" and "how" of introductory courses.

Second, his assertions that the "world is probabilistic rather than deterministic" and the "statistics is the means by which different interpretations of data can be evaluated" are consistent with current notions about the philosophy of mathematics (Tymoczko, 1986) and the philosophy of mathematics education (Ernest, 1991). From these complementary philosophical positions, his point that "as mathematics is the language of science, statistics is the logic of science" is not only tenable, but consistent.

Third, while Dr. Ruberg's focus is on the introductory collegiate courses in statistics, most of what he is suggesting should be part of the experiences of all students, not just those who go to college. In fact, given the increasing importance of data representation and analysis, NCTM's *Curriculum and Evaluation Standards* proposes that the mathematics curriculum in U.S. high schools needs to include the fundamental ideas of collecting survey data, randomness, variability, sampling distributions and hypothesis testing, and so forth. If this recommendation were to be implemented, then the initial collegiate courses could build on this background. Of course, such a change is not feasible today, but we should work together to assure that it happens tomorrow.

Finally, I would like to emphasize the importance of both collecting and making sense of "real" data. Sensemaking, which is at the heart of all mathematics, is of critical importance to everyone

during the initial exposure to statistics. However, most people rarely experience the whole process of raising a question, gathering data, and trying to make sense of the information collected. Statistical formulas were invented to help in the interpretation of information. They will only be understood as important if one has experienced a situation that needs to be interpreted and if one sees how the use of that formula helps in the interpretation.

In conclusion, all citizens need to see that with statistics, as Dr. Ruberg states, we can "address challenging problems and issues that impact the well-being of all members of society by moving from uncertainty, to experimentation and data collection, to analysis and to what is likely to be best for all of us."

References

- Ernest, P. (1991). *The philosophy of mathematics education*. Bristol, PA: The Falmer Press.
- Landwehr, J.M., Swift, J., & Watkins, A.E. (1987). *Exploring surveys and information from samples*. Palo Alto, CA: Dale Seymour Publications.
- Mathematical Association of America (MAA). (1991). *A call for change*. Washington, DC: National Academy Press.
- National Council of Teachers of Mathematics (NCTM). (1989). *Curriculum and evaluation standards for school mathematics*. Reston, VA: Author.
- National Research Council. (1991). *Moving beyond myths*. Washington, DC: National Academy Press.
- Tymoczko, T. (1986). *New directions in the philosophy of mathematics*. Boston: Birkhäuser.

Discussions continue on page 9

Conference Report

1991 Applied Statistics Conference

Karl E. Peace

Organizer

The Biopharmaceutical Section of the ASA sponsored two tutorials and a two-day short course at the 1991 Applied Statistics Conference. Dr. Suresh Rastogi, Director, Divisions of Biometrics and Epidemiology (DBE), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA), gave a tutorial on the statistical aspects of evaluating biological products. Dr. Michael Kenward, Professor, University of Reading and Dr. Byron Jones, Professor, University of Kent at Canterbury, gave a tutorial on repeated measures analysis of categorical data. Dr. Kenward, Dr. Jones, and Dr. Harji Patel, Senior Scientist, Berlex Laboratories, co-taught the short course on the Design and Analysis of Crossover Trials including utilization of baseline measurements.

The tutorials and short course were moderated by Dr. Karl E. Peace, who is the Biopharmaceutical Section Representative to the Applied Statistics Conference.

The conference was held at the Sands Hotel in Atlantic City, and was very successful. Attendance was high for both tutorials and short courses. Total attendance was in excess of 340.

Minutes of August 20, 1991, ASA Biopharmaceutical Section Business Meeting

Gladys Reynolds opened the Business Meeting by announcing the new officers for 1992: Bruce Rodda, Mark Scott, Chris Gennings and Nancy Flourmoy. She thanked Executive Committee members Camilla Brooks, John Schultz, Karl Peace, and Sharon Anderson, who had helped her during her term of office.

JeAnne Burg reported on the Section's activities at the Joint meetings. There were four Invited Paper sessions (two assigned and two special), three Special Contributed Paper sessions and six Contributed Paper sessions including 41 papers. Last year at ENAR there were five Section-sponsored sessions. At the 1992 Winter Conference, there will be two sessions. Dan McGee is pursuing future sessions for the upcoming March Meeting.

Karl Peace reported on the Applied Statistics Conference. In 1991, the Section sponsored three sessions: Statistical Considerations in the Evaluation of Biological Products by S. Rastogi; The Analysis of Binary and Categorical Repeated Measurements Data by M. Kenward and B. Jones; and Equivalence Testing by Sharon Anderson. In addition, there was a two-day tutorial on the design and analysis of cross-over trials by B. Jones, M. Kenward, and K. Peace. Gladys Reynolds thanked Karl for his successful programs for many years.

Pat O'Meara reported on the 1991 meeting at Ball State. There were more than 150 attendees for the Hands-On Data Analysis meeting. A. Zellner was the banquet speaker. The Proceedings will include the session on Statistical Methods in Phase I Clinical Trials. S. Ruberg organized this session. F. Rockhold is the Program Chair for next year, and three sessions are being organized by J. Herson, R. Pittman, and R. Obenchain.

Nick Teoh reported that there were nine roundtable luncheons this year. Two new Work Groups have formed: Population Pk Modelling headed by Lianng Yuh with more than 12 participants; and Epidemiology (head not stated).

Nick Lange reported on the Longitudinal Data Analysis Symposium. The symposium was successful with the Section receiving about a \$2000 profit. It took about two years to arrange and was useful in bringing together academic and industry statisticians. The Section will be soliciting topics for future symposiums.

Pat O'Meara reported on the ASA Literacy Program and how the Section could better participate in the program. The program is ongoing in several areas around the country but the local cost of \$20,000—25,000 is beyond the scope of the Section. A committee was formed to determine what the Section could do. Members are Pat O'Meara, Mike Boyd, Lillian Kingsbury and John Lambert.

Bob Starbuck shared with the attendees that the PMA Biostatistics Steering Committee is conducting a survey regarding statistical outreach programs which were sponsored by PMA members. The survey will obtain information on what activities are working, what the benefits are, and for what level of student are the programs being conducted. The results will be made available to the Section.

Camilla Brooks discussed the issue of the Section sponsoring students at the meetings. Plans are being formulated for next year. The questions being addressed are: in which meetings do we wish to offer sponsorship; who should be sponsored, students or faculty; how should the students be selected; and how should this program be advertised?

Gladys Reynolds and Camilla Brooks asked for people to work with them on the issue of training statisticians. One concern is the

number of graduate students who do not complete their degree. Suggestions included the Section working with companies to obtain scholarships and to let the government agencies know how important it was to fund the training of statisticians.

Sharon Anderson presented the Section funds. A total of \$25,620 is available. Gladys Reynolds presented a Section budget of \$15,200 for 1992. We spent \$1020 in 1991. The 1992 budget included: \$7,000 for the Quarterly; \$1500 for the membership drive; \$150 for letterhead; \$1,750 for awards; \$400 for telephone; \$2,000 for travel and \$2,400 for the membership questionnaire. The membership is expected to increase and should be over 1,000 by the end of the year.

JeAnne Burg reported on the Committee on Meetings. This is a new committee to coordinate all of the Section meetings including the liaison committee members activities. The committee will identify deadlines for meetings, publish more information about the Section activities, tell how to participate in *Amstat News*, and encourage wider participation. The committee is also preparing a section of the Manual for Operations.

John Schultz presented the activities of the Awards Committee to stimulate an interest in the Section. The other committee members are Camilla Brooks, Lillian Kingsbury, and Tuli Cnaan. The committee will make awards for the best presentation of a contributed paper at this meeting based on audience evaluations. The first place prize will be \$500 and a plaque while the second place prize will be \$250. The winners will be identified by late October. Awards will also be made for the best publication, but this is a more laborious process. The committee is working out the best way to handle the review process.

Gladys Reynolds mentioned that a Membership committee had been formed with John Schultz, John Lambert and Gary Neidert as members. They will work on a charter. Activities will include working on a flyer outlining the benefits of belonging to the Section. More members are needed in order to have more than one representative to the Council of Sections. Any ideas should be sent to Gary. A member of the audience asked how one joins the Section. One just needs to send a check to the ASA office indicating that it is for membership in the Biopharmaceutical Section.

Louise Ryan updated the members on the Section's new publication. Tuli Cnaan will be the Editor of the publication. The new publication is a combination of a newsletter and a journal. The first issue will be next January and will contain items of interest, session notices, who is doing what and notice of upcoming events. The first paper will be by M. Zelen titled "Ethics and Clinical Trials: Some Neglected Issues." The paper will also have discussants. There will be several issues a year. The cost of the publication will require about one half of the yearly dues. The second year will see an expansion to include short technical articles and more communication by fellow Section members.

Gladys Reynolds thanked Tuli Cnaan for the wonderful job she is doing on the publication. She also announced that there will be a survey to determine the needs of Section members and soliciting volunteers. The meeting adjourned at 6:55 p.m.

Submitted by Sharon Anderson

Secretary Treasurer

ASA Biopharmaceutical Section

January 9, 1992

Discussion

Concepts in Introductory Courses and Relation to Total Quality Management

Robert V. Hogg

University of Iowa

First, there are two technical errors that I, as a teacher of statistics, must correct. The p-value is not "a probability, if you will, that the null hypothesis is true." It is a probability that, under the null hypothesis, the test statistic will be at least as extreme as that particular observed value of it. That is, it is the tail-end probability (beyond that observed value) of the distribution of the test statistic *assuming that the null hypothesis is true*.

The sentence after the "no free lunch" remark is wrong. The word *probability* should be inserted twice to read "If the probability of one type error is decreased, the probability of the other will be increased."

Now, let's address the main theme of the paper: the first course in statistics plus a few remarks about statistical education in general. I agree with almost every suggestion that Ruberg makes. I might say things differently—and have—but there are also many other individuals and groups who are preaching the same thing. Unfortunately, Ruberg, by his own admission, is not aware of much of this other activity. I do not mean to fault him as he is not in academia, and I am pleased that someone like Steve (in industry) would take the time and effort to learn as much as he has about statistical education.

In June 1990, the University of Iowa, in cooperation with the American Statistical Association, held a workshop on statistical education in which the participants concentrated on the first course. There were four publications resulting from this.

1. The November 1990 issue of *Amstat News* carried a listing of the major recommendations.
2. *The American Statistician*, November 1991, included the commentary Education: Improvements Are Badly Needed," which Ruberg mentions.
3. There was a summary of the workshop in the *Newsletter* of the Statistics Division of the American Society for Quality Control.
4. A major report entitled "Towards Lean and Lively Courses in Statistics" will appear in MAA's *Statistics for the Twenty-First Century*. Hopefully this publication, which includes other worthwhile thoughts on the teaching of statistics, will appear in the next six months.

In this short discussion, let me simply remark on a few of the major items in Ruberg's paper, which are fairly consistent with his thoughts.

Goals: The aim in a first course is to develop critical reasoning skills necessary to understand our quantitative world. The focus of the course is the process of learning how to ask appropriate questions, how to collect data effectively, how to summarize and interpret that information, and how to understand the limitations of statistical inferences. Statistical thinking is central to education.

Scientific Method: Students should appreciate how statistics is used in the endless cycle associated with the scientific method. We observe Nature and ask questions, we collect data that shed light on these questions, we analyze the data and compare to what we previously thought, and new questions are often raised. It *has* proved to be an exciting process for many years; but, most of the time, the students do not experience this excitement in our classes. There is a consensus among statisticians that statistics offers a unique and useful way of looking at the world and helping to solve real problems—or to exploit opportunities, but that statistics teaching in colleges and universities fails to communicate the potential, the utility, or the joy of discovery through investigation.

Variation: The introductory courses, to be most effective,

cannot be taught solely as mathematics, but must be data oriented, getting the students involved in projects having statistical components. That is, students and faculty must understand that statistics is a study of variation, and in it we try to find patterns despite the fact that the data points generally do not precisely fall on those "theoretical curves" due to "noise."

Statistical Thinking: Statistical thinking is different from that to which most students have been exposed. The ideas of uncertainty and variability are either ignored or dealt with poorly in everyday discourse and even academic study. Statistical thinking may even be counter-intuitive, as illustrated by the appearance of "hot streaks" and "momentum" or the notion that the "sophomore jinx" is a mysterious plague of nature.

Projects: Advocate projects in which students collect their own data and analyze them in written reports. Such projects combat apathy by allowing students to work with data that they find interesting. Moreover, projects give students experience in asking questions, defining problems, formulating hypotheses and operational definitions, designing experiments and surveys, collecting data and dealing with measurement error, summarizing and analyzing data, communicating findings, and planning "follow-up" experiments that are suggested by their findings.

Experimental Design and Surveys: Two topics in which we should stress the importance of getting quality data. Also there should be discussion about the ethics of experimentation and the distinction between observational and experimental investigating.

Teaching: Teachers are often unimaginative in their methods of delivery, relying almost exclusively on traditional lecture/discussion. They fail to take into account the different ways in which different students may learn, both individually and in groups, or the many possible modalities of teaching. They also fail to use the wide variety of simulation, experiments, and individual or group projects which can make statistics come alive while simultaneously enhancing their understanding.

Textbooks: There are some textbooks that are "breaking out of the mold." I mention only three: *Statistics* by Freedman, Pisani, and Purves; *Statistics: Concepts and Controversies* by Moore; and *Statistics for Business: Data Analysis and Modelling* by Cryer and Miller. I am encouraged by what I see and I urge teachers of statistics to look at these and other newer books.

Let me end this discussion on what I see as a beginning of a healthy trend, namely the application of Total Quality Management (TQM) to education from K-12 through graduate work. That is one of the reasons I really like the Cryer/Miller approach because there is a great deal of TQM throughout their text. This movement is only starting, but I do believe that it will encourage quality improvement in education.

The Department of Statistics and Actuarial Science at the University of Iowa has made a commitment to improving our programs. Many of us use Mosteller's one-minute papers in which a few students each class period will give us feedback by recording what they thought was the most important topic of the day, the muddiest, the one they want to know more about, and any other suggestion for improvement. These comments are addressed the next period. In addition, a few are using Quality Improvement Teams and meet with them once a week for their suggestions.

In our applied M.S. program, we are proposing a two-semester sequence "Quality Improvement Through Statistical Thinking" which will run concurrently with the two standard sequences Probability/Mathematical Statistics and Regression/Design. In this new course we will start with the quality Philosophy and Shewhart Control Charts, but also try to tie the other two sequences together through projects, reports, etc.

In closing, let me thank Steve for the fine job of calling the Biopharmaceutical Section's attention to this important topic. I know that many of you truly believe in improving statistical education, and I am pleased that I had the opportunity to make these comments about it.

Software Review

StatXact Version 2.0/Cytel Software, Cambridge, Massachusetts

Reviewed by Keith Soper
Merck Research Laboratories

StatXact is a program for exact nonparametric inference on IBM PC-compatible microcomputers. The authors, Mehta and Patel, have published extensively on efficient algorithms for exact nonparametric inference, and StatXact is a remarkable tour de force in terms of speed and ease of use. This review summarizes my impressions of StatXact Version 2.0 based on just over a year's experience using it for analysis of animal drug safety studies. I also preview some features of the new StatXact Turbo version. StatXact version 2.0 requires an IBM PC compatible microcomputer with DOS, 640K RAM, and a hard disk (math coprocessor highly recommended). StatXact Turbo requires, in addition, a '386 or '486 processor and at least 2Meg RAM.

The phrase "exact inference" refers to a class of statistical procedures based on conditioning arguments. Conditional on some event, the distribution of a statistic is completely specified, so in principle "exact" p-values and confidence intervals can be constructed. The great majority of nonparametric procedures fall in this class, including binomial confidence intervals and Wilcoxon signed rank tests (for one sample), Wilcoxon and permutation score tests (for two samples), logrank and Wilcoxon-Gehan tests (for censored data), Fisher's exact, chi-squared, and likelihood-ratio tests (for R X C tables), and trend tests (for stratified 2 X C tables). StatXact's unique contribution is to provide exact inference for a great many commonly used tests, including all in the above list. Version 2 provides p-values to test the null hypothesis in all cases, and in addition, provides exact conditional maximum likelihood estimates and confidence intervals for the common odds ratio (in stratified 2 x 2 tables) or common trend parameter (in stratified 2xC tables).

Exact analysis is useful when the accuracy of asymptotic approximations is in doubt because the data set is small, events studied are rare, the data are highly skewed, or ranked data have many ties. For example, the following data on maternal drinking and congenital sex organ malformations (Graubard and Korn 1987) is taken from Chapter 4 of the StatXact manual:

Alcohol Consumption (drinks/day)

Malformation	0	< 1	1-2	3-5	≥6	Total
Score	0	0.5	1.5	4	7	
Present	48	38	5	1	1	93
Absent	17066	14464	788	126	37	32581
Total	17114	14502	793	127	38	34574

StatXact provides the exact one-sided $p = 0.0168$ by trend test, as well as the usual asymptotic approximation $p = 0.0052$. The computation required under 15 seconds on my 20MHz 386 machine with 4Meg RAM. PROC FREQ in PC SAS does not yield an exact p-value for this table. StatXact Version 2 was not able to compute the complete probability distribution (list the probability of all 968 possible scores), but StatXact Turbo did so in under six minutes.

StatXact is remarkably fast, and in those occasions when an exact analysis is not feasible, StatXact provides Monte Carlo p-values by sampling from the permutation distribution. Importance sampling is available for some tests. A 99% confidence interval on p is shown

and continuously updated as the sampling progresses. The asymptotic p-value is always provided for comparison.

Quite a bit of effort has gone into making StatXact easy to use. I was able to run analyses after only 30 minutes including installation and tutorial. Analyses can be specified as either EXact, MOnTe Carlo sampling from the permutation distribution, or ASymptotic. Each analysis requires 2-5 keystrokes. Possible commands at each point appear at the bottom of the screen. Data can be entered from the keyboard or input from ASCII files, either as tables or individual cases. It is easy to pool over strata or temporarily delete specified rows or columns. StatXact is designed for interactive use, but has a batch mode useful for running a series of analyses (for example, analysis of each tumor type in a rodent carcinogenicity experiment).

There is a help facility that allows one to ignore the manual, but the manual is beautifully done and well worth reading. Each statistical procedure is introduced with a "theory and methods" discussion describing motivation, definition, and guidelines for application. Detailed citations to the statistical literature are given. Twenty-eight real data sets are analyzed, with frequent panels explaining how to read the screen. These data sets are included with the software.

StatXact provides only nonparametric inference, so for many it will not be the sole software system used for data analysis. Some way to import data directly from PC SAS would be useful for SAS users. I understand StatXact Turbo will have this. Nonparametric procedures not currently available in StatXact include Peto's test for animal carcinogenicity experiments, exact logistic regression, sample size calculations for discrete data, and adjustment for multiplicity of tests performed. To my knowledge, the last procedure is available only in the SAS PROC MULTTEST.

StatXact employs the network algorithm, and runs 20-100 times faster than the direct enumeration software I was using previously. My first thought on being asked to alpha-test StatXact Turbo was the "Turbo" is redundant. But the Turbo version is quite a bit faster than StatXact version 2. Comparing four populations (rows) in the 4x5 contingency table

1	1	0	1	1
2	3	1	0	0
0	6	5	4	2
0	0	5	5	1

by exact Kruskal-Wallis test on my PC required 1 hour, 40 minutes with Version 2, compared with 8 minutes, 20 seconds with StatXact Turbo. I understand that the Turbo version runs substantially faster on a PC with additional RAM or with a '486 processor. Aside from running much faster, StatXact Turbo eliminates the limit of 5 rows or columns for tables in StatXact Version 2, can import data directly from PC SAS files, and can run on a network.

To summarize, StatXact provides the first simple and fast way to do exact non-parametric analysis of highly skewed or sparse data, or to examine whether approximate asymptotic analyses are accurate. It is easy to use, handles data sets generally considered too "large" for exact inference with incredible speed, and is beautifully documented. This kind of quality does not come cheap (\$495.00 for Version 2), but I have used it almost daily in my work analyzing animal drug safety experiments. There is a discount for academic institutions, or a network version of StatXact can be used to bring down the price per user.

Reference

Graubard BI and Korn EL (1987), Choice of column scores for testing independence in ordered 2 x K contingency tables, *Biometrics*, 43, 471-476.

StatXact is a product of Cytel Software Corporation, 675 Massachusetts Avenue, Cambridge, MA 02139.

Discussion

Statistics Education: A Framework and Foci

Ramanathan Gnanadesikan

Rutgers University

Dr. Ruberg's article deals with a topic that has been receiving a great deal of attention over the past decade. The issues and objectives he highlights are by now widely accepted as legitimate ones, and a good deal of effort is underway on curriculum reform as well as development of new teaching materials that are in tune with this reform movement. The Quantitative Literacy Project (a collaborative effort by the National Council of Teachers of Mathematics and the American Statistical Association) that focused on pre-college level statistics education, and the subsequent spawning of several NSF funded projects to develop so-called *activity-based statistics* educational materials for the undergraduate level, are just two examples. In fact, statistics and statisticians were ahead of the general mathematical community by at least a few years in recognizing the need to improve and indeed to fundamentally modify the teaching of statistics, including the introduction of statistical concepts and tools very early in the K-12 curriculum. The reform in mathematics education more broadly, when it came along, was able to benefit from and exploit this head start by incorporating and expanding on the thinking and the materials that had been developed by statisticians. Apparently, however, as Dr. Ruberg himself acknowledges, his article was written without any efforts at reviewing any of the available information (e.g., a number of publications of the Mathematical Sciences Education Board of the National Academy of Science) or detailed curricular materials mentioned above. The 1992 Winter Conference of the American Statistical Association was devoted to statistics education and the papers/discussions presented there constitute a good source for current thinking and practices.

Although considerable work has been and is currently underway, there is more that needs to and can be done. For instance, the delineation of a natural framework for statistics education could be helpful both as a convenient, rational structure for developing and discussing curricula and as a means for identifying focal points for and lacunae in pedagogical emphases. Viewed in this light, Dr. Ruberg's paper (which is admittedly more a potpourri of topics deemed to be important than an attempt at identifying a framework) stays within the confines of traditional thinking in its emphasis of probabilistic bases and inferential aspects of statistics. In what follows, I suggest a framework that is natural for statistics and then discuss some specific technologies/tools that should permeate the statistics curriculum instead of being treated as specialized topics confined to a single course or perhaps two.

Since statistics is largely *data science*, a natural framework for organizing a curriculum would consist of: (1) planning the *collection* of data, (2) methods for *analysis* of data, and (3) *interpretation* of data and their analyses. Under the first item belong the basic concepts of sample surveys and designed experiments, including randomization, randomized responses, replication, blocking, and the efficient study of several factors. This would also be the place to emphasize the importance of understanding the context of the data and the substantive problem that is to be addressed through the use of statistics. The second category is the one that receives the lion's share of most current curricula although the methods are often taught as specialized, individual courses (e.g., time series, regression analysis, nonparametric methods, multivariate analysis, etc.) rather than as inter-related topics with cogent common themes and goals. The analytical methods range from simple summaries to subtle modeling techniques and strategies. The resurgence of the

data analysis movement in the 1960s resulted in many new methods over the next three decades, and these have been melded into many if not all statistics courses. The third piece, concerned with understanding of and insights into data and with communicating these findings to others (with varying degrees of expertise/knowledge about statistics), is one that needs considerably more attention in the curriculum than it currently receives. Formal statistical inference procedures of all ilk are perhaps the main focus of what is covered traditionally here, but these are often only a small part of what is involved and needed for effective understanding and communication. Diagnostics and the flexible use of different methods and analyses, so as to facilitate serendipity in discovering unanticipated structure and patterns, as well as the process of synthesizing the results of different analyses of the same body of data, are all important principles and practices to inculcate in students.

The above tri-part, data-centered framework can be useful, at times, in designing the contents of a single course. For example, even in a single course for non-majors, some exposure to all three parts of the framework is important to achieve. The framework could also be very important for designing an entire curriculum or sequence of courses so as to ensure a balance among the critical corner stones of an education in statistics. Clearly, for instance, in thinking about what an undergraduate major in statistics or a Master's degree "should know," the framework can be useful. The extent and depth of coverage of material structured by the tri-part framework would and should vary with the level (e.g., non-major vs major).

What about specific technologies/tools that need to be emphasized? I can think of at least three: (1) activity-orientation, (2) computing, and (3) graphics. The recognition of visualization and "kinetics" (hands-on) as important modalities of learning, in addition to the traditional oral mode, has brought to the fore the role of these technologies in education, in general, and statistics education, in particular. A key feature about all three of these is their broad relevance and the need to have them permeate the statistics curriculum. For instance, graphics are currently often relegated to "descriptive statistics" but they have a role that can and should cut across the entire curriculum ranging from elucidating basic and often "abstract" concepts (e.g., law of large numbers) to analysis, model building, and communication of results. Similarly, statistical computing (under which umbrella I include simulation and a host of resampling methods in addition to the standard methodological algorithms) should be an integral part of most of the courses taught and not treated solely as a specialized topic for just some students. As to activity-oriented statistics, there seems to be clear evidence that "doing" not only provides illustrative experience with data analysis, but is a valuable way of learning some of the more abstract concepts (e.g., mutual independence, central limit theorem, and the interpretation of confidence intervals) through "discovery." A concomitant benefit of the "hands on" activity would be the learning of the limitations of the methods.

Despite the spate of interest and activity in statistics education in recent years, one area that has received scant attention to date is graduate education, especially at the Ph.D. level. The role of research and the preparation for careers in which research and specialized knowledge will play significant parts, brings certain new dimensions into the debate on appropriate curricula for such students. However, for pedagogical purposes many of the issues raised in connection with the statistics curriculum at earlier levels are likely to be relevant at the graduate level as well. It is inevitable and certainly long overdue that this last bastion not be any more of a "sacred cow" than the other levels of education have been. It behooves us as statisticians to take a fresh look at assessing the contents of the graduate curriculum sooner rather than later.

Discussion

What Experience in Teaching Shows Us

Spencer M. Free

Newtown Square, Pennsylvania 19073

I want to compliment Steve for accepting the challenge of discussion teaching statistics. I want to congratulate him for completing the task with his thought-provoking paper. I like his emphasis on the first course. Perhaps I like that emphasis because it prompted me to think about my introductory courses in statistics and what they taught me.

My professors were George Snedecor and David Finney. All the classmates were working together to share the real data experiences, and we were anxious to use our new skills, and the new ideas we acquired immediately. I taught my first course with Jack Youden and my students were industrial chemists. Many of them brought data with them to share.

Even when I taught mathematical statistics, I worked hard on explanations with real data examples and emphasized cooperation among peers. I made communicating among students a high priority. I continued to teach statistics courses in local academic programs throughout most of my industrial career. I do not consider myself qualified to be a member of the teaching profession. However, my frequent exposures provided opportunities to think about what was successful for me. My students encouraged the use of real data examples, and they all agreed the minimal extra effort needed for real data added to their understanding. Better yet, they would talk to others about statistics and generate their own enthusiasm.

I was prepared to find this theme in Steve's very positive discussion. It is my impression that he is suggesting a first course in understanding some basic uses of statistics before the first course in the more rigorous mathematics of statistics. Steve's emphasis in the first basic uses course would include 7 or 8 subjects that he carefully described. I like his choices. The quantity is small enough for one semester. The range is broad enough for students to gain a good feeling about some topics and a cautious feeling about others. I like his explanations even better. He suggested ways to explore each subject. His suggestions all provide material that a student could understand and soon communicate to others. Obviously, I think communicating to others can be one of the keys to understanding and enjoying statistics in the early learning phase.

I hope Steve is trying to tell his audience that many of the students that complete his first course will have the motivation to go on to the second course. He didn't say it, but I will. The basic understanding found in the first course will make the next more mathematical course earlier to understand. Students will know how to recognize numbers for the Y_{ij} 's that are in the formulas.

I sense his enthusiasm in the paragraphs under the section "After the Second Course." He sees the students off to a good start with multiple reasons to continue. He provided several excellent suggestions for emphasizing the philosophy of statistics in place of the mathematical rigor. He does not remind his readers of the tough grind between really getting involved in a training program and completing the requirements. That is avoided because he knows the pleasures that are enjoyed by those who complete a formal training program and become active in our profession.

Steve's last phrase in that section is "accurately communicating the results to clients." From my perspective, that can be one of the major goals of formal training. I have tried to place the emphasis in my teaching on developing enough understanding to confidently communicate statistical findings to others.

Discussing this paper prompted me to think about the changes I have made to teach statistics for understanding and practical use.

Biopharmaceutical Report, Summer 1992

My career started when there were just a few text books. Now we have a constantly increasing range of text and reference books. Early, I suggested books to help somebody understand a problem. Now, I can identify chapters in books that will be more specific. When my computing facility was a desk calculator, I tried to recommend one good omnibus approach. Today, I often suggest at least two approaches, so my contact can experience a broader perspective of the problem. I like to suggest the best statistical solution and an alternative for more understanding and better communication. It is great to be active when there are so many useful resources readily available.

Steve is writing for the Biopharmaceutical Section. We were a Committee in 1966, a Subsection in 1968 and Section in 1981. Much has changed in that short interval. Our discussions with the biological scientists have changed. We are no longer explaining what statistics is all about. We are describing what it can do for them and many times expanding to show them what more we can do. We once had to train new statisticians to think about the nuances in the biological sciences. Now many arrive with more formal training including some course work that anticipated biological applications. I sense that for many students, the availability of so many more statistics course options has been at the expense of opportunities to meet Steve's recommendation for more exposure to real problems, for my desire to have students explain their findings to others.

I know Steve will agree that much of the teaching has been done very well. We should all express our appreciation to those who have worked so hard to provide today's training programs. We can make suggestions because there is something in place that gives us confidence and a desire to change. Steve had provided some very helpful suggestions for changes that can lead to improvements.

Discussion

Statistical Anxiety, Statistical Reasoning, Active Learning, and Intimate Teaching

Thomas E. Bradstreet

Merck Research Labs

Introduction

Statistical education has become the subject of much focused thought by our profession in recent years. After some real soul searching, statisticians have begun addressing questions like "Why is introductory statistics difficult to learn? And what can we do to make it easier?" (Watts, 1991). One author concluded that improvements in statistical education are badly needed (Hogg, 1991). Another suggested that we may have to statistically re-educate the North American industrial work force to stay competitive in the future (Weldon, 1988). Therefore, I am pleased to see that statistical education is the topic for discussion in this issue of the *Biopharmaceutical Report* and wish to thank Dr. Ruberg for beginning the discussion. I will comment on statistical anxiety, the choice (or balance?) between statistical reasoning and statistical methods in introductory statistics courses, and learning statistics through active student participation. I will add to the discussion some thoughts on "intimate teaching." Finally, I want to comment on some technical issues in the paper.

Statistical Anxiety

As Dr. Ruberg suggests, people are afraid of statistics. Motivation for why statistical thinking should supersede statistical methods or at least precede them in any introductory course for nonstatisticians is provided by an understanding of "statistical anxiety." Statistical anxiety is defined as "the feelings of anxiety encountered when taking a statistics course or doing statistical

analyses, that is, gathering, processing or interpreting data." (Cruise et. al., 1985). It is common for teachers of non-calculus based statistics courses to encounter varying degrees of anxiety or fear in non-statistics majors. This anxiety and fear may become more intense in classes for graduate students, because these students realize that analyzing data will be an important part of their research. Students who lack quantitative skills or confidence in their quantitative abilities may be especially prone to anxiety which, if excessive, interferes with learning (Chmielewski and Chmielewski, 1983). Students are often "scared at the prospect of taking a statistics course" long before enrolling. This condition is also common among the nonstatistical members of biopharmaceutical research teams in industry (Bradstreet et. al., 1992).

Statistical anxiety may have its roots in math anxiety. Math anxiety is the "feelings of tension and anxiety that interfere with the manipulation of numbers and the solving of mathematical problems in a wide variety of ordinary life and academic situations." (Murdock, 1983). It is easy to see how math anxiety could preempt statistical anxiety. In fact, math anxiety is likely to be the primary cause of statistical anxiety. Since many undergraduate and graduate students are required to take few, if any, mathematics courses following high school, students often conclude that they cannot successfully complete a course in statistics, for which sophisticated mathematical knowledge is perceived by the students as a prerequisite for success. Even though statistics should not simply be presented as a branch of mathematics, particularly at the beginning level (Hogg, 1991), the connection between the two subjects in the minds of nonstatisticians is inescapable.

Statistical Reasoning versus Statistical Methods

The most critical point in developing any introductory statistics course for nonstatisticians is deciding whether to teach statistical reasoning, statistical methods, or both. Recently, there has been quite a bit of support for teaching statistical reasoning (concepts) instead of teaching only statistical methods (computations), as evidenced by several of the presentations at the 1992 ASA Winter Conference on statistical education. The emphasis in this type of course is on thinking about research issues in a statistically sound and practical fashion. Students learn how to formulate and ask the right questions, how to construct testable subject matter hypotheses, how to choose the right study design, how to collect data effectively, how to choose statistical methods, how to summarize and interpret information, how to present study results, and how to understand the limitations of statistical inference (Sahai, 1989; Hogg, 1991; Bradstreet et. al., 1992). Since it is not the intention of such a course to produce a batch of statisticians, it is important that the computations performed by the students be reserved for selective reinforcement of data-analytic and data-interpretation concepts (Marks, 1989; Bradstreet et. al., 1992). Also, the use of complex formulas and mathematical notation should be minimized. The students need to grasp the concepts of statistical reasoning and decision making; they need not be able to fluently read and write large amounts of statistical notation. I am in general agreement with Dr. Ruberg's idea of teaching statistical thinking prior to statistical methods, although I propose that an effective balance of the two can be achieved in a first course rather than putting off most of the methods until a second course as he suggested. I also propose that statistical reasoning should continue into the second course.

Learning Statistics Through Active Student Participation

Dr. Ruberg suggests that students should be encouraged to actively investigate questions of interest through statistics projects. Further, statistics labs should be set up so that students can process data (once they collect it), plot data, perform simulations,

and the like. He also suggests that all graduate level statistics students need to do some analysis of real data accompanied by interpretation and presentation to fellow students or members of departmental faculty. These are good ideas. Workshop-based courses, particularly for nonstatisticians, are becoming more popular and have proven to be effective (Wolfe, 1982; Shannon, 1988; Bradstreet, 1992; Rossman, 1992). The traditional teaching method is the lecture-discussion-homework-test approach. Lectures do not work nearly as well as many teachers of statistics like to think. Students learn better by active involvement; they learn to do well only what they practice doing; they learn better if they have experience applying ideas in new situations (Cobb, 1991). Projects give students experience in asking questions, defining problems, formulating hypotheses and operational definitions, designing experiments and surveys, collecting data and dealing with measurement error, summarizing data, analyzing data and communicating findings, and planning "follow-up" experiments suggested by the findings (Hogg, 1991). Teachers of statistics should rely less on lecturing and more on individual and group projects, group problem solving and discussion, written and oral presentations, demonstrations based upon class-generated data, and lab experiences (Cobb, 1991). It has been suggested that instruction in modern statistics begin with data analysis (Moore, 1992).

Intimate Teaching

One aspect of statistical education which Dr. Ruberg did not explicitly mention is the type of relationship that should exist between the teacher and the students. If this relationship is a healthy one, then quality education can take place even in the face of limited additional resources. If this relationship is unhealthy, then no amount of money and/or resources will produce a quality education. The key to "intimate teaching" is the removal of barriers between the students and the instructor (Davenport, 1984). One approach to intimate teaching is for the instructor, along with the students, to work new problems which the instructor has not solved previously. This puts the instructor "at risk" in front of the class and allows for a more intimate relationship to form between the teacher and the students. On a larger scale, the workshop approach also promotes intimate teaching if the teacher and students work together and the students are divided into small work groups (Bradstreet, 1992).

Teachers should be well prepared for class, hold a positive regard for students, and provide students with regular and specific feedback (Guskey, 1988). They should have an adequate knowledge of the subject matter, provide a teachable text and comfortable classroom (Davenport, 1984). Teachers need to know their target audience, show energy and enthusiasm in the classroom, minimize note taking and maximize thinking and discussion by providing effective handouts and previously prepared course notes, and be accessible before, during, and after the class.

Technical Issues

I do not agree with Dr. Ruberg's explanation to his colleague in toxicology that the p-value is the probability that the null hypothesis is true. In classical hypothesis testing, the null hypothesis is either "true" or "false." The p-value is more appropriately thought of as a data-dependent summary statistic which assesses the extremeness of experimental evidence in rejecting the null hypothesis (Casella and Berger, 1990). I also assert that in the strictest sense, there are no assumptions necessary to conduct a randomization test on data produced in a randomized experiment. One need only have knowledge of the randomization scheme. The randomization itself provides the basis for a test of the hypothesis that there are only random differences among the treatments (Edgington, 1987). Lastly, I agree with Dr. Ruberg that randomization is important in removing bias in the

assignment of experimental units to treatments, but I disagree that it will necessarily balance covariates between treatment groups, particularly given the relatively small sample sizes routinely used in many experiments (Friedman et. al., 1985).

Closing Remarks

One last comment is in order. In my relatively brief but quite satisfying experience of teaching, jointly with my statistical colleagues, eight classes of an introductory statistics appreciation course at Merck Research Labs, I have found the same dismal pre-course outlook on statistics in the overwhelming majority of our students as Dr. Ruberg described in his paper. Some of our students' comments prior to the course include "Statistics was my worst subject!" and "It's too abstract! What do X's and Y's have to do with the real world anyway?" as well as, "I can't do math so how can I get through this class?" and "Will this be as painful as in college?" And most of the students are terribly confused about the statistical methods to which they were exposed. But, herein lies the challenge. Having recognized and evaluated statistical anxiety in the students, we balanced statistical reasoning with statistical methods, invited active learning, and implemented intimate teaching techniques. This combination has turned around the students' attitudes towards statistics. There is a waiting list to get into the first course. Many students are requesting a second course. Dr Ruberg is correct in asserting that it is in these introductory classes that our profession has its first chance to entice the minds and spirits of students. It is indeed rare that we get a second chance.

References

- Bradstreet, T.E., Belliel, S.L., Berman, R.S., Copenhaver, M.D., Hesney, M., Holder, D., Hufnagel, K., Kersh, L., Liss, C., Neafus, R.P., Payne, J.E., Schwartz, S.W., Snively, D.B., Suchower, L.J., and Walton-Bowen, K.J. (1992). A Statistics Appreciation Course for Clinical Research Personnel. *Drug Information Journal*, 26: 31-40.
- Bradstreet, T.E. (1992). Statistical Reasoning or Statistical Methods? *Proceedings of the Biopharmaceutical Section, American Statistical Association*, presented at ASA Winter Conference, Louisville, Kentucky, January 3-5, 1992, to appear.
- Casella, G., and Berger, R.L. (1990). *Statistical Inference*. Pacific Grove, CA: Wadsworth & Brooks/Cole.
- Chmielewski, M.A., and Chmielewski, J.J. (1983). The Three R's for Teaching Statistics: Relaxation, Reduction of Anxiety, and Reinforcement of Concepts. *Proceedings of the Section On Statistical Education, American Statistical Association*, August 15-18, 1983, Toronto, Canada, 118-123.
- Cobb, G. (1991). Teaching Statistics: More Data, Less Lecturing. *Amstat News*, #182, 1 and 4.
- Cruise, R.J., Cash, R.W., and Bolton, D.L. (1985). Development and Validation of an Instrument to Measure Statistical Anxiety. *Proceedings of the Section On Statistical Education, American Statistical Association*, August 5-8, 1985, Las Vegas, Nevada, 92-97.
- Davenport, J.M. (1984). Thinking In Front of the Students — And Other Skills For Effective Instruction of Small Statistics Classes. *Proceedings of the Section On Statistical Education, American Statistical Association*, August 13-16, 1984, Philadelphia, Pennsylvania, 8-10.
- Edgington, E.S. (1987). *Randomization Tests*. New York: Marcel Dekker, Inc.
- Friedman, L.M., Furberg, C.D., and DeMets, D.L. (1985). *Fundamentals of Clinical Trials*. Littleton, MA: PSG Publishing Company, Inc.
- Guskey, T.R. (1988). *Improving Student Learning In College Classrooms*. Springfield, Illinois: Charles Thomas Publishers, Chapter 2.
- Hogg, R.V. (1991). Statistical Education: Improvements Are Badly Needed. *The American Statistician*, 45 (4): 342-343.
- Marks, R.G. (1989). Emphasizing Concepts Instead of Computations In Teaching Biostatistics. *Proceedings of the*

- Section On Statistical Education, American Statistical Association*, August 6-10, 1989, Washington, D.C., 16-17.
- Moore, D.S. (1992). Introduction: What Is Statistics? Chapter 1 In: *Perspectives On Contemporary Statistics*, D.C. Hoaglin and D.S. Moore, editors, Mathematical Association of America, MAA Notes Number 21.
- Murdock, M. (1983). Math Anxiety and Statistical Readiness In Health Sciences Students. *Proceedings of the Section on Statistical Education, American Statistical Association*, August 15- 18, 1983, Toronto, Canada, 124-125.
- Rossman, A. (1992). Introductory Statistics: A "Workshop" Approach. Presentation at Winter ASA Meetings, January 3-5, 1992, Louisville, Kentucky.
- Sahai, H. (1989). Some Problems of Teaching Introductory Biostatistics Courses to Graduate Students in Health Sciences. *Proceedings of the Section On Statistical Education, American Statistical Association*, August 6-10, 1989, Washington, D.C., 35- 39.
- Shannon, H.S. (1988). Development of A Problem-Based Course In Biostatistics. *Proceedings of the Section on Statistical Education, American Statistical Association*, August 22-25, 1988, New Orleans, Louisiana, 220-221.
- Watts, D.G. (1991). Why Is Introductory Statistics Difficult to Learn? And What Can We Do To Make It Easier? *The American Statistician*, 45(4): 290-291.
- Weldon, K.L. (1988). Statistical Re-education of Industrial Scientists and Engineers. *Proceedings of the Section on Statistical Education, American Statistical Association*, August 22-25, 1988, New Orleans, Louisiana, 96-98.
- Wolfe, F.M. (1982). A Problem-Centered Approach To Teaching Medical Statistics. *Proceedings of the Section on Statistical Education, American Statistical Association*, August 16-19, 1982, Cincinnati, Ohio, 201-206.

Rejoinder

Teaching Statistics for Understanding and Practical Use

Steven Ruberg

I would like to say that I am honored to have such a distinguished list of discussants on my essay, "Teaching Statistics for Understanding and Practical Use." Many of these individuals have been involved in statistical education for a long time and are people that I have long admired. I join Dr. Free in extending my thanks to them for advancing statistical science to where it is today. Their comments are filled with many pearls of wisdom for statistical education in the future. I am also thankful to the discussants for their specific references to programs and publications that have dealt with this issue. As I said in my essay, I am only vaguely aware of some of these initiatives but I am glad to see that my thoughts are basically in step with these programs.

I will address the technical issues first and then make more general remarks about the discussants' view points. I thank the discussants for their careful review of my essay and for pointing out a few technical errors that need to be corrected. As Dr. Hogg points out, I should have mentioned the probability of an error when discussing hypothesis testing. As mentioned by Mr. Bradstreet, there are no assumptions necessary to conduct randomization tests other than having a valid randomization scheme. I also agree with Mr. Bradstreet that randomization will not "necessarily balance covariates between treatment groups," and I did not mean to convey this in my essay—only that randomization is a very good method for trying to balance covariates, both those that are measured and those that are unknown or unmeasured.

Finally, I will address the statement that "the p-value is, if you will, the probability that the null hypothesis is true." Of course, any statistician with any amount of training knows that this is not the true definition. I used that statement intentionally to create a bit of a stir and to see what responses I would get from discussants. Two discussants provided specific definitions of the p-value. Dr. Hogg stated, "it is the tail end probability (beyond that observed value) of the distribution of the test statistic assuming that the null hypothesis is true." Mr. Bradstreet suggested that the p-value is "a data dependent summary statistic which assesses the extremeness of experimental evidence in rejecting the null hypothesis." While these two statements more precisely describe what the p-value is, they are complicated, and very much like the definition I quoted in my essay about the sample space. If I were to give these definitions to any naive client or to any group of introductory students, I feel quite certain that they would struggle with their meaning. In fact, these discussants helped to emphasize my point—sometimes we statisticians become too obscure with our clients in our quest for being mathematically or logically precise with our statements. We can turn off the audience or the client before we even have a chance to show them we can help.

Now, I am not advocating that we stop with such a simple statement about the p-value. I am suggesting that we make

statements that can be generally understood by the audience in order to help them stay with us long enough for us to get into more technical details and give more precise definitions. This certainly helped in my consulting with the toxicologist who collaborated with me on many more projects and became very adept at understanding principles and concepts.

There are a few general remarks that I would like to make about the discussants' viewpoints and some specific statements that I enjoyed. I thought that Dr. Scheaffer made a good point in saying "a key to statistical thinking is that randomness generates a predictable pattern." This is something I had overlooked, and I think it is very useful and important to teach. I also thought that Dr. Scheaffer made a good point about teaching students basic concepts about variance components. With regard to Dr. Scheaffer's comments on estimation, I would argue that even when doing exercises of an exploratory nature to get some intuition about numbers, students learn a lot about how to collect data, what assumptions are made, and how confident they are in their estimates.

I think that Dr. Hogg made a good point when he said that "statistical thinking may even be counter-intuitive." There are many examples of this, of which Dr. Hogg cited two well-known cases. I also thought that Dr. Hogg made a good comment about discussing the ethics of experimentation. His comments on Mosteller's One

Conference Report

1992 ENAR Spring Meeting in Cincinnati

Sessions Sponsored by the Biopharmaceutical Section

■ Statistical Problems in Estimating HIV Seroprevalence

Organizer: John Karon, Centers for Disease Control **Chair/Discussant:** Ira M. Longini, Jr., Emory University

Three talks were given in this session. Nicholas Jewell from the University of California at Berkeley spoke on the "Reconstruction and prediction of HIV infection rates based on AIDS incidence data." Dr. Jewell discussed the use of backcalculation as a method to reconstruct the HIV infection pattern from data on AIDS incidence and knowledge of the AIDS incubation distribution. He provided methods for incorporating nonstationarity of the AIDS incubation distribution and additional data on specific causes of AIDS diagnosis into the backcalculation technique. In addition, he discussed the effect of misspecification of the AIDS incubation distribution on the backcalculation technique.

Donald R. Hoover from Johns Hopkins University (with Alvaro Munoz and Vincent Carey) spoke on "Estimating 1978-1990 and future HIV-1 seroconversion in subgroups of homosexual men." Dr. Hoover presented statistical methods that use AIDS-free men recruited in 1984-85 to retrospectively estimate HIV-1 seroconversion rates in subgroups of homosexual men starting in 1978. For the future, he found that a seronegative 20-year-old man has a 20.2% chance of seroconverting before reaching the age of 24 years, and about a 50% chance of seroconverting before reaching the age of 55 years.

Marcello Pagano from Harvard University spoke on "Pooling blood sera to reduce cost and improve quality of HIV screening." Screening for HIV provides a measure for curbing the further spread of the virus. Effective, widespread screening, however, is prevented by its high cost and the high false positive predictive values associated with the tests. Dr. Pagano presented two new screening procedures involving the pooling of blood sera which can reduce these costs substantially. At antibody prevalences between 4 and 40 per 10,000, Dr. Pagano's proposed procedures can reduce the false positive predictive value at least 50 times and the false negative predictive value up to 40 times compared to the standard procedure.

■ Toxicity Monitoring In Clinical Trials

Organizer: Joel Verter, Henry Ford Hospital

The first talk was given jointly by Gordon Pledger and Lynn Kramer from the R. W. Johnson Pharmaceutical Research Institute and was titled, "Adverse event data: It ain't like efficacy data." The speakers presented various points of view of statisticians and clinicians concerning analyses that need or do not need to be done, and the interpretation of these analyses.

The second talk, by Christy Chuang-Stein from Upjohn was titled "a unified approach to the analysis of safety data in clinical trials." After presenting problems of having multiple p-values, no control for type 1 error, and other problems, she suggested a scoring system for safety issues. The body system is divided to k classes, and each patient has a vector of grades based on the intensity of the AE and agreed weights. The grades are compared by using a modified Mantel-Haenszel statistic looking at differences in scores between treatments.

The last talk was given by Enoch Bortey from Norwich Eaton Pharmaceuticals and was about applying survival methodology to adverse experience occurrences in clinical trials. The cumulative hazard of the occurrence of an AE is estimated by fitting a two-parameter model, where one parameter describes the rate of AE occurrence and the other is associated with duration of exposure to drug. The parameters are fitted using maximum likelihood. The method was tried on an example data set with AE's in several body systems and results were consistent across the body systems.

Minute Papers were very refreshing. I am glad to hear that we in the statistical profession are taking a dose of our own medicine in using statistical quality control concepts in our own classrooms to better instruction. Congratulations to the department of Statistics and Actuarial Science at the University of Iowa for instituting such a program and to all other departments that have done so.

Dr. Gnanadesikan mentioned the Winter Conference of the American Statistical Association, which was devoted to statistical education. I have heard many good reviews of that conference, organized by Dr. Hogg, and I hope that some proceedings are forthcoming. I do agree wholeheartedly with Dr. Gnanadesikan that hands-on activities help students to understand the difficulties of actually collecting and analyzing data and the limitations of their methods.

I thought Mr. Bradstreet made a good argument for an effective balance between teaching statistical thinking and statistical methods. Such a balance would be ideal, but I think it might be difficult to cram too much of this into a one semester course. Of course, I too agree that statistical thinking should continue into the second course and beyond. I also think that Mr. Bradstreet's citation about beginning instruction in modern statistics with data analysis is very valid and an important approach to consider even on the first day of class. I liked his suggestion that instructors work along with students on problems for which the instructor has not yet arrived at a conclusion of a solution. I think this would help the student gain an appreciation for how exploratory analysis is done or how statisticians view data in many different ways before reaching a final conclusion. I would also congratulate Tom and his colleagues at Merck Research Labs for what appears to be a very successful program in statistical education for the scientists there.

I feel that in the essay I have raised very few new ideas or concepts that have not been discussed widely in the statistics community. However, I do want to reemphasize or challenge our educators on two concepts for which there was very little commentary. The first is the use of labs in the teaching of the first course in statistics. While many commentators stress the use of examples in projects, there was very little said about the use of labs. Again, I am thinking of labs like those routinely done in science courses: formal labs of three hours per week that are done in conjunction with lectures or other information given within a classroom setting. This is one way to get hands-on experience and to tie data analysis to principles and concepts taught in the classroom. This is exactly why labs are done in biology, chemistry, and many other sciences. I do agree with all of the discussants that examples or projects need to be meaningful. It is only when students or research clients have success with their own data, their own projects, and their own questions that statistics becomes a real part of their own thinking and future use.

The second challenge has to do with Ph.D. education, for which only one discussant suggested reform. Again I will challenge our educators to have requirements in all Ph.D. programs for data analysis. Dr. Gnanadesikan emphasized that statistics is largely a "data science." If statistics truly is a data science, then real data ought to be part of the formal education.

Finally, I will conclude by commenting on two excellent ideas that I found in the discussions. The approach that I took towards statistical education, especially in the first course, was a historical one. How did our forefathers grapple with the notions of variability, central tendency, and the like? Dr. Scheaffer suggested that the course follow a more logical research process: exploratory analysis, planning consideration, probability, and confirmatory analyses. I think this is a very good idea and may help students understand not only statistics but how it fits into the scientific method. Dr. Hogg also made suggestions along these lines about tying statistics and the scientific method together.

Another approach suggested by Dr. Gnanadesikan was to take a natural framework for organizing the curriculum that consisted of planning the collection of data, the analyses of the data, and the

interpretation of the data. This is very similar to what was proposed by Dr. Scheaffer. I also found it interesting that Dr. Gnanadesikan advocated this "tri-part data centered framework" not only for individual courses but for designing entire statistical programs. I like this idea very much, and it reminds me a bit of repeating geometric patterns that form fractals, where each part of the pattern contains a replica of the whole pattern. I think that this approach within each course and across all courses would do well for students who took only one class or for students who completed a PhD in statistics.

Again, I would like to thank all of the discussants for their insights into the statistical education process. I hope that this essay and the discussions have served to emphasize to statisticians that we all teach statistics in our own way—in dealing with clients one-on-one, in teaching courses to our colleagues in laboratory science or engineers in manufacturing, or in educating students in the classroom. I urge all of us to continue our efforts in whatever capacity to bring about a more enlightened society as to the nature, practical use, and importance of statistical thinking.

Conference Reports

1992 Pharmaceutical Manufacturers Association Education & Research Institute Training Course in Non-Clinical Statistics

Tim Schofield

Merck Research Laboratories

The Pharmaceutical Manufacturers Association Education & Research Institute sponsored Training Course in Non-Clinical Statistics was held March 1-4, 1992, at the Georgetown University Conference Center in Washington, D.C. This was the second year the course was offered and it was well attended by new and experienced statisticians, as well as non-statisticians interested in the broad range of statistical applications in basic research and pharmaceutical development.

The faculty included industry and FDA statisticians. Technical presentations were offered on various topics:

- Experimental Design
- Screening Assays
- Stability Studies
- Assay Validation
- Pharmacokinetics and bioequivalence/bioavailability

Attention: ASA Annual Meeting Attendees

All ASA Biopharmaceutical Section Members are cordially invited to attend a **Wine & Cheese Reception**

Date: Tuesday, August 11, 1992
Time: 6:00-8:00 p.m.
Place: Salon G
 Boston Marriott Hotel
Sponsor: PAREXEL International Corporation

- Toxicology/Pathology
- Non-Clinical Pharmacology
- Quality Control/Assurance
- Bioassay, Immunoassay, and Drug Receptor Theory.

Many lectures focused on the scientific and practical issues encountered in each research area, along with the statistical contribution to the solution of those problems. This year's course included two non-technical sessions:

■ A panel discussion on Statistical Consulting, in which the faculty expressed their views on interacting with the scientific community and the human side of statistical consulting.

■ A session on Statistical Graphics and Data Display where effective and accurate communication of scientific results were highlighted.

In addition to the formal agenda, the faculty were encouraged to interact with participants during breaks and after-hours. Georgetown provided a splendid atmosphere for attendees to relax, socialize, and share their experiences. "Luncheon conclaves" were organized each day, during which students had the opportunity to question the faculty about specific problems they faced in their work. All elements blended together to make the Pharmaceutical Manufacturers Association Education & Research Institute Training Course in Non-Clinical Statistics a rewarding experience for students and faculty alike.

1992 Pharmaceutical Manufacturers Association Training Course for New Clinical Statisticians

Samuel M. Heft, Ph.D.
Rhone-Poulenc Rorer

On March 29—31, 1992, the Biostatistics subsection of the Pharmaceutical Manufacturer's Association presented the Fifth Annual Training Course for New Clinical Statisticians. Sixty-six students, mainly statisticians new to the clinical trials area participated in this course, which was taught by experienced faculty from the pharmaceutical industry and the FDA. Over the past five years, over 300 such statisticians have benefitted from this program.

The primary objective of this intensive two-day course is to expose technically well-trained statisticians to many of the basic elements of clinical trials in order to aid in their professional development. The course's format encourages extensive two-way interaction between the faculty and the students through the use of break-out sessions and roundtable discussions, in addition to formal presentations. Additionally, the opportunity to share experiences with counterparts at other companies has proved most useful.

The program and faculty were:

1. *Planning of Clinical Studies*—**Samuel M. Heft** (Rhone-Poulenc Rorer, Course Director)
2. *Bioavailability/Pharmacokinetics*—**Lianng Yuh** (Parke-Davis)
3. *Positive Controlled Trials & Efficacy Analysis with Missing Data*—**Sharon Anderson** (Syntex)
4. *Crossover Studies & Combination Drugs and Factorial Designs*—**Kenneth J. Koury** (Lederle)
5. *Interim Analysis & Multi-Center Studies*—**Arthur Devault** (Bristol-Myers Squibb)
6. *Assessment of Drug Safety*—**Gregory G. Enas** (Lilly)
7. *Statistical Graphics and Data Display*—**Thomas E. Bradstreet** (Merck)
8. *The FDA and the IND/NDA Statistical Review Process*—**Satya D. Dubey** (FDA)

Merck-Temple Conference on Research Topics in Pharmaceutical Statistics

The Merck-Temple Conference on Research Topics in Pharmaceutical Statistics was held on May 15, 1992 at the Ambler Campus of Temple University with 162 statisticians attending. Boris Iglewicz opened the Conference by stating that the Temple Statistics Department will commence offering biostatistics and pharmaceutical statistics courses at its Suburban Ambler campus starting with the Fall 1992 semester. This is in addition to the extensive offerings at the Temple Main Campus. Burt Holland, Department Chair, then gave a brief description of Department programs and activities. Bob Davis (Merck) in his closing remarks stated that the Merck Research Laboratories were happy to co-sponsor the Conference and hoped that this Conference can become a regular event.

The program, speakers, and brief summaries are given below:

1. *Statistical Issues in the Design and Analysis of Pharmaceutical Economic Studies*—**Joseph Heyse** (Merck Research Laboratories)

The rising awareness of health care costs has increased interest in studies with the objective of evaluating the clinical and economic outcomes of pharmaceutical products. Several illustrations of such studies were given and a summary was made of the basic statistical methods used in the design, analysis, and interpretation of quality of life and cost effectiveness studies in the presence of variability. Several research issues were suggested in the development of practical methods for combining clinical trial results with treatment costs.

2. *The Use and Value of CD4 Cell Count and other Surrogate Markers in AIDS Clinical Trials*—**Stephen Lagakos** (Harvard University)

CD4 cell count and other laboratory markers of viral load or immune competency are being used increasingly in clinical trials of persons infected with HIV, the virus that causes AIDS. The potential advantages of these markers, when used as surrogates for clinical progression, is that the process of drug evaluation and approval can be substantially shortened. However, if the markers are poor surrogates for treatment differences then ineffective drugs could be approved and or effective drugs could be overlooked or used suboptimally. As an illustration, it was demonstrated that the CD4 cell count is not a perfect surrogate marker for the effectiveness of AZT. The consequences of this finding were then discussed.

3. *Some Remarks on Statistical Issues in Population PK/PD Modeling*—**Sanat Sarkar** (Temple University)

Several different approaches have been proposed in the literature for the purpose of population PK/PD modeling. The statistical methodologies involved in these approaches were summarized. Special emphasis was placed on discussion of the estimation of the PK parameters with nonlinear mixed effects models (NONMEM). The lack of basic knowledge of the statistical properties of such estimates was discussed and several research undertakings were mentioned.

4. *Group Sequential and Bayesian Approaches for Evaluating Equivalence*—**A. Lawrence Gould** (Merck Research Laboratories)

Clinical trials are often carried out to evaluate the bioequivalence of two or more treatments. The standard 80-120 rule declares two treatments bioequivalent if the 95% confidence interval for the relative effect is within (0.8, 1.2). An interval of (0.9, 1.25) when the target interval is (0.8, 1.2) only suggests what the conclusion should be, but does not support it definitely. A group sequential type approach is suggested for bioequivalence studies. A bayesian approach to evaluating equivalence has also been previously studied. The latter approach turns out to be a special case of the general class of group sequential designs.

5. *Meta-Analysis: Problems and Promises*—**Colin Begg** (Memorial Sloan Kettering Cancer Center)

The distinguishing features between meta-analysis and conventional statistical analysis were listed as: component studies differ organizationally; absence of access to raw data; sampling

issues; relative credibility and quality of component studies. Variation in component studies can be due to differences in the source population, the treatments administered, study design, protocol compliance, and end-point definition. As a result, resolution of heterogeneity and study quality are two key issues in meta-analysis. Options are to include all studies, take a "high" quality subset, or perform a quality weighted average. A strength of meta-analysis is the capacity to develop a very precise analysis from the combined studies. Weaknesses include the potential for naive aggregation of dissimilar studies, and the risk of bias.

6. *Statistical Issues in Pharmacokinetics*—Francis Hsuan (Temple University)

The definition of "bioequivalence" has recently been questioned. Instead of it being based on the means of bioavailability parameters, it is suggested that it be based on approaches that insure the interchangeability among different brands of medications. In concurrent PK1/PK2 analysis, the objective is to model the interdependency structure between two PK curves taken simultaneously. Many existing methods for analyzing such data are unsatisfactory. The physiological meaning of clockwise and anticlockwise hysteresis was explained. Two issues that came up were: (1) inefficient algorithms, and (2) not all PK/PD curves can be modelled by existing methods.

Upcoming Events

American Statistical Association Joint Meetings—Boston, August 1992

Program Highlights

The preliminary program for this year's joint meetings was published in the May issue of *Amstat News*. We would like to draw your attention to the sessions sponsored by the Biopharmaceutical Section.

There are three invited sessions organized primarily by the Section:

- 7. Biopharmaceutical Studies from the 1988 National Maternal and Infant Health Survey organized by Gladys Reynolds from the Centers for Disease Control.
- 113. Comparison of Approaches to Population Pharmacokinetic Modeling: A Case Study using Clinical Data, organized by Denise J. Roe from the University of Arizona.
- 216. Statistical Methods for the Detection of Interactions between Drugs, organized by Scott S. Emerson from the University of Arizona.

Three other invited sessions are organized primarily by other sections and the Biopharmaceutical Section is jointly sponsoring them:

- 4. Multiplicity and meta-analysis in clinical trials, organized by Demissie Alemayehu from American Cyanamid Company.
- 69. Quality management for clinical research in the pharmaceutical industry, organized by Christopher Barker from Syntex Research.
- 247. Monitoring complex clinical trials, organized by Nancy Geller from the National Heart, Lung, and Blood Institute.

Forty-nine papers will be presented in eight contributed papers sessions sponsored by the Biopharmaceutical Section. These will be on:

- 31. Longitudinal analysis and repeated measures.
- 65. The analysis of clinical trials.
- 91. Some issues in equivalence and bioequivalence studies.
- 147. FDA session on special statistical issues.
- 169. Some issues in study design and management.
- 192. Issues in clinical trials.
- 249. Issues in dose-response and drug combination studies.

On Monday, August 10, there will be one poster session sponsored by the Biopharmaceutical Section.

Biopharmaceutical Report, Summer 1992

Luncheon roundtables sponsored by the Section will be on Tuesday, August 11, and are detailed below.

The Section wishes to thank Daniel McGee from Loyola University for organizing an excellent program.

Biopharmaceutical Roundtable Luncheons in Boston—Sign Up Early!

Nick Teoh

Abbott Laboratories

The Biopharmaceutical Section has scheduled ten roundtable luncheons for this year's conference. There will be a wide selection of statistical topics ranging from those that are relatively problem specific to some that cover a broad spectrum of issues. Many of the topics are currently being actively researched and developed. Participants can look forward to an opportunity to discuss directly with someone with expert knowledge of the respective areas. The luncheons also provide an informal setting to interact with one's peer group in the biostatistical profession. Since the luncheons are well attended events, early registration is encouraged in order to assure that attendees are able to participate in the roundtable discussion of their choice. For those who would like to plan ahead for these events, the following is a complete list of the roundtable luncheons:

- *Meta-Analysis*—Jonathan B. Skinner, Abt Associates.
- *Bayesian Methods for Clinical Trials*—Donald A. Berry, Duke University.
- *Change-from-Baseline and Other Response Parameters*—George Y. Chi and James H.M. Hung, FDA.
- *Designs for Phase I/II Studies*—Lianng Yuh, Parke-Davis.
- *Missing Observations in Intent-to-Treat Analysis*—Satya D. Dubey and Mohammad F. Huque, FDA.
- *Analysis and Design Issues for Large Multicenter Clinical Trials*—David S. Salsburg, Pfizer.
- *Computer-Assisted NDA Review (CANDAR)*—Gary L. Neidert, The Upjohn Company.
- *Exact Inference*—Cyrus R. Mehta, Cytel Software Corp./Harvard University.
- *Role of Biomarkers in Validating Adverse Drug Reactions*—Jerome Wilson, Warner-Lambert Company.
- *Utilization of Optimization Methods in Drug Research and Development*—Chris Gennings, Medical College of Virginia.

1992 Applied Statistics Conference

Organizer: Karl E. Peace

The Biopharmaceutical Section of the ASA will sponsor two tutorials and a two day short course at the 1992 Applied Statistics Conference. Dr. Richard Chiacchierini, Director, Biometric Sciences Division, Center for Devices and Radiological Health (CDRH), Food and Drug Administration (FDA), will give a tutorial on the statistical aspects of evaluating medical devices and radiological health products. Dr. Karl Lin, Statistical Applications and Research Branch (SARB), Biometrics Division, Center for Drug Evaluation and Research (CDER) (FDA), Dr. Sehin- Chung Chow, Associate Director and Head, Biostatistics Department, Bristol-Myers-Squibb U.S. Pharmaceutical Group, and Dr. J. P. Liu, Statistical Scientist, Berlex Laboratories, will give a tutorial on the statistical design and analysis of stability studies.

The tutorials and short course will be moderated by Dr. Karl E. Peace, who is the Biopharmaceutical Section Representative to the Applied Statistics Conference. The conference will be held at the Sands Hotel, Atlantic City, NJ, December 14-18, 1992.

ASA Biopharmaceutical Section Executive Committee—1992

Immediate Past Chair

Gladys H. Reynolds, Ph.D.
Mathematical Statistician for Minority Health
Office of the Director
Centers for Disease Control
1600 Clifton Road, N.E., Mailstop A50
Atlanta, GA 30333
(404) 639-3318
(404) 639-2195 fax

Chair

Camilla A. Brooks, Ph.D.
President, CB Quantitatives, Inc.
PO Box 2572
Chapel Hill, NC 27515
(919) 493-5408 phone and fax

Chair-Elect

Bruce E. Rodda, Ph.D.
Vice President, Biostat & Data Management
Bristol-Myers Squibb Pharmaceutical Research Inst.
PO Box 4000
Princeton, NJ 08543-4000
(609) 921-5776
(609) 921-5740 fax

Secretary-Treasurer

JeAnne R. Burg, Ph.D.
Chief, Exposure and Disease Registry Branch
Division of Health Studies, ATSDR
1600 Clifton Road, Mailstop E31
Atlanta, GA 30333
(404) 639-0561

Section Financing

John Schultz, Ph.D.
The Upjohn Company
Unit 9165-32-2
200 Portage Road
Kalamazoo, MI 49001
(616) 385-7427
(616) 329-5548 fax

Program Chair

Daniel L. McGee, Ph.D.
Department of Preventive Medicine
Loyola University Medical Center
2160 South First Avenue
Maywood, IL 60153
(708) 216-6038
(708) 216-4117 fax

Program Chair Elect

Mark Scott, Ph.D.
Director, Biometrics & Medical Systems
Clinical and Medical Affairs
ICI Pharmaceuticals
Office Wing 3
Routes 202 & 141
Wilmington, DE 19897
(302) 886-8495
(302) 886-2442 fax

Work Group Coordinator

Nick Teoh, Ph.D.
Group Leader, Clinical Statistics and Systems Development
Abbott Laboratories D-426/AP9A
Abbott Park, IL 60064-3500
(708) 937-4451
(708) 938-6001 fax

Chair of the Midwest Biopharmaceutical Statistics Workshop

Patrick D. O'Meara, Ph.D.
Director, Statistical Services Division
624 Peach Street
P.O. Box 80837
Lincoln, Nebraska 68501
(402) 476-2811
(402) 476-7598 fax

Representative, Applied Statistics Conference

Karl E. Peace, Ph.D., FASA
President, Biopharmaceutical Research Consultants, Inc.
4600 Stein Road, Suite B
Ann Arbor, MI 48105
(313) 663-4440
(313) 663-7797 fax

Publications Officer

Chris Gennings, Ph.D.
Biostatistics Department
Medical College of Virginia
P.O. Box 32 MCV Station
Richmond, VA 23298-0032
(804) 786-9824
(804) 371-8482 fax

Editor of Biopharmaceutical Report

Avital Cnaan, Ph.D.
Merck Research Labs, BL3-2
Merck & Co., Inc.
West Point, PA 19486
(215) 397-7015
(215) 397-2931 fax

Chair of Committee on Advisors to FDA

Vern Chinchilli, Ph.D.
Associate Professor, Department of Biostatistics
Medical College of Virginia
1101 East Marshall Street
PO Box 32, MCV Station
Richmond, VA 23298-0032
(804) 786-9824

Council of Sections Representative

Edward S. Nevius, Ph.D.
Division of Biometrics
Food and Drug Administration HFN-713
5600 Fishers Lane
Rockville, MD 20857
(301) 443-4594

Council of Sections Representative

Nancy Flournoy, Ph.D.
Associate Professor, Mathematics and Statistics Dept
American University
Clark Hall, Rm 211
4400 Massachusetts Ave. NW
Washington D.C. 20016
(202) 885-3127
(202) 885-2013 fax

Liaison Activities

Helen Bhattacharya, Ph.D.
Director of Biostatistics
Sanofi Pharmaceuticals, Inc.
40 East 52nd Street, 13th floor
New York, NY 10022

Biopharmaceutical Section Executive Committee—1992 (continued)

Executive Committee

Nguyen V. Dat, Ph.D.
Associate Director of Biometrics
Smith Kline Beecham
P.O. Box 1510 M/C FF0605
King of Prussia, PA 19406
(215) 270-6277

Lilliam Kingsbury, Ph.D.
Director of Biostatistics
Bio-Pharm Clinical Services
512 Township Line Road
Blue Bell, PA 19422
(215) 283-0770
(215) 283-0733 fax

John Lambert
Director, Biomedical Operations
Sandoz Pharmaceuticals, Inc.
Route 10
East Hanover, NJ 07936
(201) 503-6914

Gary Neidert, Ph.D.
Director of Clinical Data Management
The Upjohn Company
Unit 9165-298-139
301 Henrietta Street
Kalamazoo, MI 49001
(616) 329-8591
(616) 329-5579 fax

Jerome Wilson, Ph.D.
Director of Biostatistics and Data Management
Warner-Lambert
170 Tabor Rd., Room 3015
Morris Plains, NJ 07950
(201) 540-2422
(201) 540-4300 fax

Akbar Zaidi
CDC Mathematical Statistician
Division of SPD/HIV
Center for Prevention Services
1600 Clifton Road, N.E.
Atlanta, GA 30333
(404) 639-2562
(404) 639-2555 fax

Let's Hear from You!

If you have any comments or contributions, contact:
Dr. Avital Cnaan, Editor, Biopharmaceutical
Report, Merck Research Labs, BL3-2,
Merck & Co., Inc. West Point, PA 19486
Telephone: (215)-397-7015 Fax: (215)-397-2931

The Biopharmaceutical Report is a publication of
the Biopharmaceutical Section of the American
Statistical Association.

Layout designed and produced by
Alison Stern-Dunyak, American Statistical
Association, Alexandria, Virginia.

© 1992 American Statistical Association

Biopharmaceutical Report

c/o American Statistical Association
1429 Duke Street
Alexandria, VA 22314-3402

Let Us Know Your ZIP + 4

Non-Profit
Organization
U.S. Postage
PAID
Permit No. 361
Alexandria, VA