泛華統計協會

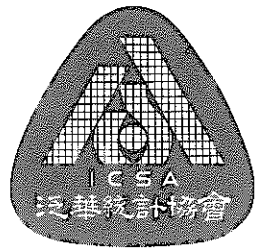
會刊

International Chinese Statistical Association

Website: http://icsa.org

Bulletin

January 2001



編者的話：

會刊是我們會員的主要交流園地，預計每年在一月及七月發行兩期，希望各位踴躍賜稿，文章以一至二頁爲主，須用中文繁體字或英文書寫，文章性質以一般性非專門學術的文章爲主，以前或本期會刊內的各篇短文都是很好的範例，稿件如採用，我們希望能由作者安排打字，完稿的上，下，左，右邊(margin)至少要有四分之三英吋，頁碼離底邊二分之一英吋，打字打在 8" x 11" 的白紙上。爲統一起見，若以英文書寫，請用Microsoft Word打字，中文繁體字請用Microsoft Word with Valupack Fareast feature打字。稿件的截止日期是六月十五日及十二月十五日。截止日期後收到的將列爲下一期的稿件。

刊內付有本會的申請表(application form)，其中會員動態內的著作(publication)以一年內的新作品爲限。

從1994年度起本會酌收徵才廣告費一頁U.S.$200或半頁U.S. $120。

對於以上的一些構想，如果您有任何建議，請與泛華協會執行長丁乃迺迪(地址見下)聯絡，以期這份刊物更爲完善。

2000 會刊通訊錄編輯人員

Publication Committee

Website: http://www.icsa.org

I.C.S.A. c/o Yi Tsong, Ph.D.
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EXCUTIVES AND MEMBERS OF THE COMMITTEES OF ICSA 2001

EXECUTIVES

President:	Chao Agnes Hsiung (2001)
Past President:	Chien-Pai Han (2001)
President-elect:	William W.S. Wei (2001)
Executive director:	Yi Tsong (2001-03)
Treasurer:	H.-M. James Hung (2001-03)

BOARD OF DIRECTORS

I-Shou Chang (1999-01), Ngai Hang Chan (2001-03), Chen-Hsin Chen(2001-03), Rongdean Chen (1999-01), Jianqing Fan (2000-02), Chien-Pai Han (1999-01),
Agnes Hsiung (2000-02), Mei-Ling Lee (2001-03), Guo-Ying Li (2001-03),
Ker-Chau Li (2000-02), Karl K. Lin (2000-02), Dan-Yu Lin (1999-01),
Nancy C. H. Lo (1999-01), Jun Shao (2000-02), X.Don Sun (2001-03),
Mei-Cheng Wang (2000-02), William W.S. Wei (2001-03),
Zhiliang Ying (1999-01),Frank Shen (2000-02, Biometrics Section Representative)

STANDING COMMITTEES

PROGRAM COMMITTEE:
Hubert J. Chen (chair 2001; member 2001-02), Yu-Sheng Hsu (2001),
Xiang Rong Yin (2001), Ouhong Wang (2000-01)
Term of reference: to plan, coordinate and arrange the annual meeting, 2001.

FINANCE COMMITTEE:
H.-M. James Hung (chair 2001-03), Xiu-Chen(2001-03),
Wei-Ying Yuan(2001-03)
Term of reference: to oversee the budget and financial situation of the Association.

NOMINATING AND ELECTION COMMITTEE:
Mei-Cheng Wang (chair 2001; member 2000-01),
Dennis K.-J. Lin (2000-01), Jen-Pei Liu (2001-02), Frank Shen (2001-02)
Term of reference: to nominate the candidates for the President-elect and members of Board of Directors.

PUBLICATION COMMITTEE:
Zhiliang Ying (chair 2001; member 1999-01), I-Shou Chang (2001-03) James J. Chen (2000-02), Sue-Jane Wang (Bulletin),
Ker-Chau Li (Statistica Sinica), Yi Tsong (ex-officio)
Term of reference: to supervise the publication policy of the Association and make recommendations with respect to the editorial policy of various publications.

CURRENT COMMITTEES

MEMBERSHIP COMMITTEE:
Tzu-Cheg Kao (Chair 2001, member 2000-02), James J. Chen (1999-01), Rongdean Chen (2001-03), Chong Gu (2000-02), Zhaohai Li (2000-02), Xufeng Niu (2000-02), Ming Tan (2001-03), Jane-Ling Wang (1999-01), Heping Zhang (2001-03), Hung Chen (1999-01, Taiwan),
Yeh Lam (1999-01, Hong Kong), Bo-Cheng Wei (1999-01, China)
Term of reference: to recruit more new members and contact interested potential individuals and organizations.

FUNDRAISING COMMITTEE:
Jianping Dong (Chair 2001, member 2000-02), Alice Hsuan (2001-03),
Kuang-Chao Chang (2000-02, Taiwan)
Term of reference: to consider fund raising drive through individuals and corporations

PUBLIC RELATIONS COMMITTEE:
Yi Tsong (Chair 2001, member 2000-02), Naisyin Wang (2000-02),
Shi-Yong Feng (China), Sik-Yum Lee (Hong Kong),
Lung-An Li (Taiwan)
Term of reference: to contact news media and publicize ICSA activities, to serve as a liaison between ICSA and other professional organizations such as ASA, Biometric Society for joint activities.

AWARDS COMMITTEE:
Cun-Hui Zhang (Chair, 2001; member 1999-01),
Wen-Jang Huang (2001-03), Lynn Kuo (2000-02), Zhaohai Li (2001-03), Ming Tan (2000-02), Mark Yang (1999-01),
Term of reference: to accept, evaluate, and recommend nominations for ICSA various awards.

PROFESSIONAL ACHIEVEMENT COMMITTEE:
Yuan S. Chow (chair 2001; member 1999-01),
James C. Fu (2000-02), Jane-Ling Wang (2001-03),
Cun-Hui Zhang (2001-03)
Zhenhai Yang (2000-02, China)
Term of reference: to discuss ICSA Fellows and Chinese COPSS award.

COMMUNICATION COMMITTEE:
Chung Chen (chair 2001; member 1999-01), Don Sun (web),
Hubert Chen (listserv)
Term of reference: to evaluate the database and the use of internet.

CONFERENCE COMMITTEE:
Wai-Keung Li (chair), Xiao-Li Meng, Howell Tong, Kai-Tai Fang,
Fred Ho, Jianqing Fan
Term of reference: to arrange the 5th ICSA International Conference, 2001.

APPLIED STATISTICS SYMPOSIUM COMMITTEE:
Rongd Chen (co-chair), J.P. Hsu (co-chair), Jianqing Fan, Hung-ir Li,
Jun Liu, Xiaoli Meng, Vincent Shu, Donald Tong, Ruey Tsay, Andrew Xiao-Hua Zhou
Term of reference: to organize the Applied Statistics Symposium, 2001.

BOOK AND JOURNAL DONATION COMMITTEE:
Tar Timothy Chen (Chair)
Term of reference: to solicit book and journal donations and to arrange the delivery to universities or colleges in need.

LONG RANGE FINANCIAL PLANNING COMMITTEE:
Smiley W. Cheng (Chair 2001; member 2000-2003), Fanny Ki (2000-02), Frank Shen (2000-03), Naitee Ting (2000-02)
Term of reference: to plan long-term financial strategies, such as studying suitable avenues for investing our assets.

SYMPOSIUM PLANNING COMMITTEE:
WeiChung J. Shih (Chair 2001; 2000-04), James J. Chen (2000-02),
Rony Chen (2000-03), Tar Timothy Chen (2000-02),
Jiann-Ping Hsu (2000-04), Zhiliang Ying (2000-03)
Term of reference: to recommand future symposium site to the Board

STRATEGIC COMMITTEE: (all former presidents)
Chien-Pai Han (Chair 2001), Tar Timothy Chen, Jeff C. F. Wu,
Shein-Chung Chow, Kuang-Fu Cheng, Smiley Cheng, Chiao Yeh,
Yuan S. Chow, Jack C Lee, Grace Yang, Jia-Yeong Tsay, James Fu, George Tiao
Term of reference: to plan long-term strategies for the Association.

BIOMETRICS SECTION (2001)

Weichung Joe Shih (chair), James J. Chen (past chair),
H.-M. James Hung (chair-elect), Shou-en Lu (secretary),
Gang Li (treasurer),
Frank Shen (ICSA Representative 2000-02)

EXPRESS YOUR OPINION .....

Dear ICSA Members,

We added a list of some upcoming statistical meetings. In addition, the upcoming year 2001 applied statistics symposium and the 5th international conference of 2001 are sponsored by the ICSA. We'd like to notify you ahead of time and encourage your involvement by contacting the chairs of the corresponding events (details see announcement) or by sharing your research findings with the members. Your suggestions / comments are welcomed. Details inside ....

IN THIS ISSUE ...

GET INVOLVED IN NEXT ISSUE .....

Special topic – Acturial
Statistics' Delight/ 統計趣聞
Controversial statistical Issue – Bootstrapping vs. Markov Chain Monte Carlo

Get involved in the next issue by email your articles to the Editorial Board at WANGS@CDER.FDA.GOV

Editor's Page

Past Predicts Present and Future?

Statistics is born out from uncertainty, which plays an important role in many fields of knowledge. A recent counting and recounting of the US 2000 Presidential election ballots amounted to statistical error of margins quite critically. In this issue, the special topic of finance and the controversial statistical issue in active controlled clinical trials will broaden our minds on the role of uncertainty.

People tend to make use of the existing data to predict the immediate future. But, could it be present in a broad sense? As evidenced by recent Dow Jones and Nasdaq statistics, financial markets are ever more volatile and changing over time. The Futures Market research is vital. Model justification, taking into account random fluctuations, requires the use of statistical methods for testing its appropriateness. Statistical tools frequently used in finance literature of time series, stochastic volatility and Bayesian are discussed with their motivations behind.

The drug approval process in the United States is in place to assure that drugs available to the American public are effective and safe. As more and more drugs are approved, it may no longer be ethical to continue the practice of placebo-controlled studies. A new drug may be compared to aspirin to test for its effectiveness in preventing or treating thrombolytic and stroke patients. This type of trials is the so-called active-controlled studies. Those trials, which showed that aspirin is effective, are the placebo-controlled trials.

In the column of Controversial Statistical Issue, several serious, however, entertaining articles, e.g., "Non-inferiority: A Dangerous Toy?", depict philosophical dilemma and conceptual difficulties in conducting active-controlled studies for showing that the new treatment is not unacceptably worse than the active control agent by some pre-specified margin. The trick is to link the new treatment from the present trial with the placebo in the past trial. The big question is can such a "not unacceptably worse" claim lead one to infer that the new treatment would have been better than no treatment or the placebo had the placebo been in the present active-controlled trial with reasonable scientific evidence?

As the number of our contributing writers increases by the issue, it is as exciting as ever to put together the work of statisticians from the US, Asia and Europe. Some statistics organizations are showing enthusiasm in our Bulletin. To build on this, we are happy to exchange the meeting announcements with other organizations, e.g., the Society for Clinical Trials, to publicize our organization. We begin by publishing a meeting calendar in this issue. We hope you enjoy this issue.

Sue-Jane Wang

Editor-in-Chief

MESSAGE FROM THE PRESIDENT

January 2001

Dear ICSA Members:

The ICSA is moving into the twenty-first century. Undoubtedly, this is an era of information. We are facing huge amount of data, generated from almost every field of sciences. How to extract useful information and transfer into knowledge will be the responsibility of the 21st century statisticians. We should feel lucky as a part of the exciting discipline.

The ICSA has done an excellent job in the past decade. Last year the ICSA has made some big progress under the leadership of Professor Chien-Pai Han, especially in building bridges between ICSA and the other statistics community. Through the efforts of Chien-Pai, Tim Chen and many of our members, we obtained the encouragement from the president of ASA to nominate ICSA members as candidates for ASA president-elect. This year we will continue to interact with other statistical societies, not only in the North America, but also in the pacific region.

Bridging will be the key word in developing many of our programs. For example, the editor of ICSA Bulletin, Dr.Sue-Jane Wang, has done a great job to create a new style, which I believe will bridge the ICSA members from different regions. This year we will make effort to enhance our Web site. Internet is no doubt the most efficient way in global communication. Any suggestion to enhance the content of ICSA web pages is highly appreciated.

Our discipline has shown a big impact to the industry in the North America. ICSA members should help other regions to establish linkage among industry, government and academics. This can be gradually achieved by establishing collaboration among statisticians from different regions. Workshops and conferences across the regions could be a starting point. In the workshops or conferences, a forum to discuss new developments in statistical science can be formed and valuable interdisciplinary activities can be organized.

A good infrastructure will be essential for ICSA to become an efficient organization to all members from different regions and disciplines. I will encourage members to submit their proposals to establish new chapters or sections. With chapters established in different regions, ICSA will become a truly international statistical society.

To enhance the skills of ICSA members in career relevant areas, continuing education will be maintained and enhanced through short courses and training programs offered across the regions. The short courses organized by the Applied Statistics Symposium Committee have been recognized to be a successful program. This kind of program will also be activated in other regions besides in North America.

As for our publications, according to the Editor-in-chief of Statistica Sinica (SS), Professors Ker-Chau Li and Yi-Ching Yao, the submission to SS is growing steadily. More high quality research papers, no matter in methodology or application, are welcome submitted to SS.

As you know, the term of our Executive Director (ED), Dr. Naitee Ting, ends last December. Our new Executive Director, Dr. Yi Tsong, has been elected. Dr. Ting has contributed a lot to ICSA. He and Dr. Tsong have made a very smooth transition. Dr. Tsong has always been very active. We are lucky to have him to be our new ED. If you have any suggestions about ICSA's activities, you can either e-mail me (hsiung1@nhri.org.tw) or Dr. Tsong (tsong@cder.fda.gov).

Best wishes for a very productive new year,

Chao Agnes Hsiung **President**

Special Thanks from The Editorial Board

The Editorial Board would like to thank Dr. Chien-Pai Han, our past President, for his timely support during the preparation of this issue. We are also indebted to Dr. Timothy Chen, our President of 1999 for his enthusiastic and timely contributions.

If you have a new idea and are interested in joining us, please send your C.V. including your plan to the Editorial Board WANGS@CDER.FDA.GOV for consideration.

We encourage your active involvement in the ICSA Bulletin. Every effort counts.

Minutes from ICSA Membership Meeting on Wednesday, August 16, 2000, 6:00-7:00 P.M. Room 210, Convention Center, Indianapolis, IN

Chair: Chien-Pai Han

Attendees: About 70 ICSA members

Minutes: Naitee Ting

1. Agree on the proposed agenda

   Agreed.

2. Agree on the minutes from the previous membership meeting (published on ICSA Bulletin, July 2000, p. 3-6).

   Agreed. Naitee indicated that in case members finding errors in the minutes, please notify him for changes.

3. Further discussion on issues from the previous meeting.

   No further discussion.

4. ICSA Awards

   Chien-Pai presented Distinguished Service Awards to:

   T. Timothy Chen, for his
   - Service on the Board of Directors and on various committees of ICSA.
   - Efforts as the organizer of the 1999 ICSA Applied Statistics Symposium.
   - Significant contributions and effective leadership while serving as the President of the ICSA in 1999.

   Ching-Shui Cheng, for his
   - Service on the Board of Directors and on various committees of ICSA.
   - Effective editorship as the Chair-Editor of Statistica Sinica for three years.

5. Report from the president (Chien-Pai Han)

   Chien-Pai first introduced the President Elect, Agnes Hsiung, to all members. He then thanked the Board Directors, Committee members, the Executive Director and the Treasurer for their contributions to ICSA. The term for the current Executive Director (Naitee Ting) and Treasurer (Xiu Chen) will end by end of 2000. They will be transitioned to the next Executive Director and Treasurer later part of this year.

   This has been a very prosperous year for ICSA. Throughout this year, ICSA works on internal and external activities. Internal activities include Applied Statistics Symposiums (we had a very successful 2000 Symposium at New Jersey, the planning of 2001 Symposium is in good progress), preparation of the 2001

International Conference, publication of the 1999 Symposium Proceeding, the 2000 member Directory, and others. External activities include co-sponsoring programs with Caucus for Women in Statistics, mutual announcements with IISA (International Indian Statistical Association), and supporting JSM. Chien-Pai was invited to participate in the COPSS meeting this year. It shows that ASA becomes to recognize the importance of ICSA. At the same time, ICSA members are encouraged to participate and contribute to ASA activities so that the mutual relationship can be further strengthened.

On Sunday, the Board approved a new committee – Long Range Financial Planning Committee. This committee will study the potential of investing ICSA funds. The committee will include Smiley Cheng (Chair), Frank Shen, Fanny Ki, and Naitee Ting.

6. Business Report

   6.1 Executive Director (Naitee Ting)
   Naitee first thanked ICSA for the opportunity to work with members. From his point, the primary work up to now has been the database update. In the past half a year, labels were printed by Smiley Cheng because the old ICSA printer was out of order. Recently, we transferred to the new database on web (late June, early July). The July Bulletin was sent out using labels printed from the new system. Some members received the July Bulletin, which indicated the new system passed the first test.

   6.2 Treasurer
   Xiu Chen could not make to the JSM. The most recent treasurer report can be found in the July Bulletin (p. 70-72). Note that the Symposium account is not included in this report.

   6.3 Statistica Sinica (Ker-Chau Li)
   A written report can be found in the July Bulletin (p. 13). Ker-Chau presented the review time (in months) for papers received and the acceptance rate. He encouraged members to submit more applied papers. In the future, we hope to establish a system so that papers can be submitted on web.

   6.4 ICSA Bulletin (Sue-Jane Wang)
   The January and July Bulletins have reflected the new changes. Future Bulletins will follow the format of these two. In July Bulletin, the special topic is on statistics application in survey/poll with its implication to Presidential election taken place in Taiwan and those to be held in the United States in year 2000, and the controversial statistical issue is the use of Bayesian statistics in clinical trials. Sue-Jane also hopes to recruit more members to the Editorial Working Committee and encourages members' participation.

   6.5 Committees
   6.5.1 Executive Director Search Committee (Agnes Hsiung)
   Agnes reported that the new Executive Director will be Yi Tsong, and the new Treasurer will be James Hung. Board has approved both appointments. Their term will be January 1, 2001 through December 31, 2003.

6.5.2 Program Committee (2000 JSM Banquet)
Ouhong Wang works with members at Indianapolis to help with the ICSA desk and the banquet. We hope all members and potential members will join the banquet. The Program Committee includes Ouhong Wang (Chair), Hung-Ir Li, Wei Shen and Mei-Cheng Wang.

6.5.3 Nominating and Election Committee

ICSA 2000 Election Results

President Elect:	WEI, William W. S., Temple University
Board Directors:	CHAN, Ngai Hang, Carnegie Mellon University
	CHEN, Chen-Hsin, Academia Sinica, Taiwan
	LEE, Mei-Ling Ting, Harvard University
	LI, Guo-ying, Chinese Academy of Sciences
	SUN, Don X. Bell Lab, Lucent Technologies
Biometrics Section Chair-Elect:	
	HUNG, Hsien-Ming James, FDA

6.5.4 Membership Committee
Tzu-Cheg Kao worked with the committee members to review the ASA directory against the ICSA directory. If there is a Chinese name appear on the ASA, but not on the ICSA, then s/he is a potential ICSA member. The Membership Committee identified a list of about 200 potential ICSA members. Tzu-Cheg will then organize the list and send an invitation letter (prepared by the President of ICSA) to each of the potential members and invite them to join ICSA.

6.5.5 Communication Committee
Communications Committee maintains the website and listserv. The website has been updated periodically. One can find various information about ICSA including symposia and conferences at the website. The website address is

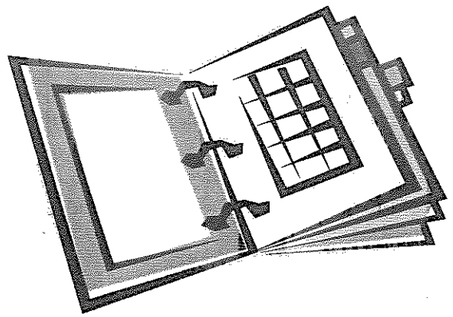
www.icsa.org.

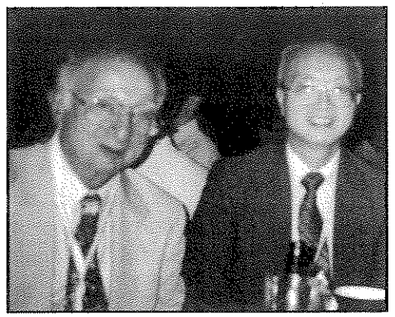
6.6 ICSA 5th International Conference
Conference Chair is W.K. Li from Hong Kong University. The conference will take place in August 2001 at Hong Kong. For details, please refer to July Bulletin pages 57, 58, and check the ICSA home page www.icsa.org.

6.7 Applied Statistics Symposium
Co-Chairs of the 2001 Symposium are J.P. Hsu and Rong Chen. Since neither J.P., nor Rong was at the membership meeting, Jianqing Fan (2001 Symposium Committee member) reported the current progress: The 2001 Symposium will take place June 8-10 in Congress Plaza Hotel, Chicago. Both the program subcommittee and the local subcommittee are working hard to prepare for the Symposium. For more information, please refer to p. 54-56 of the July Bulletin. If there is any questions, comments, suggestions or ideas, please contact the Co-chairs.

7. Other Items

In 2000, there are 4 members elected as ASA Fellows – Danyu Lin, Xihong Lin, Suojin Wang, and Heping Zhang. We also have a member won the COPSS award – Jianqing Fan.





Dr. Marvin Zelen and Dr. Chien-Pai Han at the karaoke Dinner Party

Report of 2000 Joint Statistical Meeting Committee

The Program Committee organized the 2000 JSM banquet and managed the ICSA information booth during the JSM in Indianapolis.

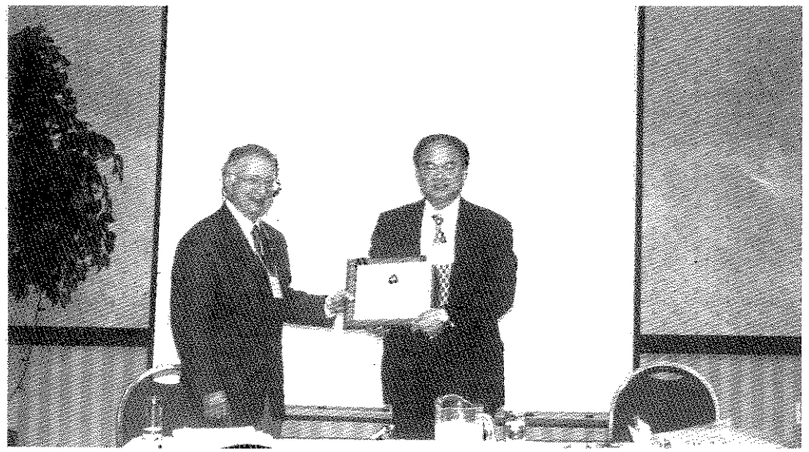
The information booth was at a good location in the convention center, surrounded by the Exhibit Hall, e-mail terminals, and conference rooms. It promoted the existence of our association, exhibited by-laws, publications and past ICSA activities, and sold tickets to the Wednesday evening banquet. It became the home base for our members during the 4-day event, and constantly drew large crowds. Several new members were recruited during the JSM, and numerous other people solicited information regarding the association and various ICSA-sponsored activities (symposium, international conference, etc.). Many members, volunteers, and ICSA officials contributed to its success. Exceptionally noticeable are Hung-Ir Li, Wei Shen, Mei-Cheng Wang, and Ouhong Wang, who form our Program Committee; and Naitee Ting, Yi Tsong, Chien-Pai Han, and our talented artist, Karen Lai, daughter of Hung-Ir. Her imaginative and colorful posters no doubt played a pivotal role in catching people's eyes.

The climax of the Program Committee-organized activities was the Wednesday evening banquet. More than 150 people showed up for the ICSA traditional event. The number exceeded everybody's estimate considering this year's JSM was in Indianapolis. It even beat some previous attendance when JSM was held at more popular locations, thanks to the outstanding efforts of our volunteers manning the information booth. The banquet provided an excellent opportunity for members and potential members to get to know each other and network. The food was excellent, price was reasonable, and the karaoke and jokes were very entertaining. Although it was a little crowded due to the unexpected attendance, it's a party full of fun! We owe our thanks to Naitee Ting and Yi Tsong, our MC and DJ for the evening, and Gordon Lan, who contributed unparalleled audio-visual expertise.

Ouhong Wang
Program Committee Chair

Statisticians, Statistical Science and the Future

Marvin Zelen
Harvard University



Keynote speaker, Professor Marvin Zelen of Harvard University, receiving certificate of appreciation from 2000 ICSA Applied Statistics Symposium Chair, Dr. Jia-Yeong Tsay

I am honored to be invited to speak at the Tenth Anniversary of the International Chinese Statistical Association. The formation of this Association and the many papers presented at this Symposium reflect the growing and important influence of scholars with Chinese heritage on our field. Without the influx of students and scholars from the Pacific Rim countries, our field, and American Science in general would not be as vigorous as it is today. The Chinese tradition of respect for scholarly achievements has encouraged many talented young people to enter our profession. May this trend long continue.

Last night was a fun night, unlike the usual banquets sponsored by our statistical organization. The talk by Henry Lee was illuminating. I was particularly impressed that he travels with a bodyguard. I guess friends come and go-but enemies accumulate. Someone in his position can make many enemies[1].

My first acquaintance with a Chinese statistician is when I was a student at the University of North Carolina in Chapel Hills many years ago. P.L. Hsu had been a faculty member at Chapel Hill but had left before I arrived. A group of students were organized to write up his lectures on Multivariate Analysis. I was part of that group. It was my first introduction to the subject.

During the next many years, I have had several students, collaborators, and colleagues from the Pacific Rim countries—especially the Peoples Republic of China. They taught me a few new English acronyms such as ABC and FOB. My friend LJ Wei refers to himself as FOB ("Fresh off the boat"). In 1979, I was invited to lecture in the PRC on clinical trials in a course sponsored by the World Health Organization (WHO). Each province in China sent one student who was supposed to return to their province and give the same lectures to others. I also gave seminars at the Cancer Hospital in Beijing and at several medical schools in Beijing and Shanghai. Up to that time, no randomized clinical trials had ever been carried out in China. However, I did learn that before the Japanese War, there had been a comparison of two therapies by assigning the therapies to alternate patients. However, the study was stopped because it was regarded as unethical.

I also met several professors of epidemiology. A small group had written a book on Biostatistics. However, the book contained no authorship, as the professors were reluctant to appear too prominent. I would hope that this situation no longer persists.

When asked for a title for my talk several months ago, I chose the most general title I could think of – "Statisticians, Statistical Science and the Future". With such a title I felt free to lecture on almost anything.

I prefer to use the term Statistical Science to describe our field. By Statistical Science I mean the application of statistics, probability, mathematics and computing to advance our understanding of a subject matter field. I refer to the practitioners of Statistical Science as Statistical Scientists – not statisticians. The terms statistics and statisticians have an ancestry when statistics were concerned with "political arithmetic". Political arithmetic dealt mainly with the study of vital statistics for the purpose of administration by governments. This is far removed from how statistical science is practiced today. It is noteworthy that many university departments of statistics have been re-named departments of statistical science. The oldest such Department located in University College, London was re-named the Department of Statistical Science several years ago. When the main field of application is in the biomedical sciences, we may often describe this activity as Biostatistical Science and its practitioners as Biostatistical Scientists.

Biostatistical Science is enjoying unparalleled developments. The need and demand has never been greater – especially in the United States. Studies carried out by the National Research Council in the U.S. have concluded that biostatisticians and epidemiologists are in the shortest supply among all health-research professionals. We need only look at any of the current issues of statistical journals to evaluate the influence that the practice of biostatistical science has on new statistical methodology. In my view, biostatistical science is at the cutting edge of many new developments in statistics. This research is mainly motivated by problems in the Health Sciences. It reminds us that statistical theory cannot be separated from the practice of statistics. When they are separate, the theory is likely to be of little consequence and the practice runs the risk of being unsound.

This new century has been described as the "Information Century". The widespread availability of computing has lead to the creation of many new databases of all kinds. However, there is a distinction between data and information. Converting data into information requires insight, skill and training in the theory and practice of statistics. Our every day lives are being affected by predictions of weather, trends in the stock market, the results of the census, reports on new therapies for diseases, etc. I believe the mark of an educated person in

this new century will be in ability to reason with numbers. In nearly all medical schools, students are required to satisfy a biostatistics requirement. I foresee the day when all undergraduates will be required to take at least one course in statistics or a course devoted to reasoning with numbers.

The growing demands in the health sciences, government and the financial sector will create a demand for statistical scientists, which we are not prepared to meet. However, there is a bright side!-As competition for statistical scientists increases, salaries will climb. This is true not only in industry but in the universities and research centers as well. I know if at least one research center, which provides new recruits with $100,000 in discretionary funds.

The U.S. is influential throughout the world, by virtue of being the largest single commercial market. Many countries are greatly influenced by activities and events n the U.S. The broad reliance of the health sciences on statistical scientists in the U.S. is influencing similar activities in other countries. Nearly all multi-national pharmaceutical companies have statistical staffs—in some instances these are quite large. Governments and industry in continental Europe are beginning to hire larger numbers of statistical scientists. However, I believe there will be tremendous growth, providing many new opportunities, in the Pacific Rim countries. For example, our Department is working with one of the Japanese universities to have visiting faculty teach courses in Biostatistics; this summer (July, 2000) there will be a three week summer session in Taipei on Biostatistical Science. Although there is only space for 150 students, more than 300 have applied to attend. I expect that similar activities will begin in Mainland China. During the next few years, I predict there will be many U.S. faculties visiting the Pacific Rim Countries to teach courses in Biostatistics.

Despite the larger salaries and the increased employment opportunities, we are not attracting sufficient numbers of well-qualified American students to our graduate programs in Statistical Science. This has provided opportunities for international students to come to this country to study. As we all know, the great bulk of these students are from the Pacific Rim countries. Many of the students are well-trained in mathematics and do well in their graduate studies. Nearly all attempt to remain in this country and are prepared to settle in the U.S. However, for many, the language skills in English are not good. It is important to recognize that an effective Statistical Scientist—whether in the University or industry must be a very good communicator—in both written and oral communication. It is important to recognize that the communication problem is a major problem for those from the Pacific Rim countries. We should encourage the Statistical Scientists, in which English is not their first language, to concentrate very early in their careers, to make up for this deficiency. Perhaps there is a role for the ICSA to take a leadership role in this activity.

One bright spot in Statistical Education is that about 5-6 years ago, statistics was introduced in the high school curriculum. It has been a great success with more than 20,000 high school students taking the Advancement Placement Exam in Statistics every year. The number of high school students studying statistics is growing very fast. These students represent a group who are likely to take college courses in statistics and some will seek a statistics major. Yet there are relatively few Departments of Statistics in the U.S. Statistics courses will be taught in the Mathematics and Social Science Departments. However, statistics is

not mathematics and studying statistics in a social science department may not be completely satisfactory. As a results we have some statisticians calling themselves Mathematical Statisticians or Applied Statisticians. (One group does not deal with data—the other group does not relate to theory.) Such descriptions "Mathematical" or "Applied" are outmoded and should be discarded. The goal is to train students who are well-grounded in theory and practice. I believe such training can only be done in Departments of Statistics. Unfortunately not every higher educational institution has a Department of Statistics. I would hope that in the future new Departments of Statistical Science will be created having as one of the main goals to carry out undergraduate education in statistics and numerical reasoning. This could be one of the goals of our profession in the new century.

In 1982, at a meeting of the International Biometrics Society, I was invited to participate in a program entitled, "The Future of Biostatistics". My address was published the next
year in Biometrics with discussion. In my talk I stated, "The future of biostatistical science will be intimately related to computing". I went on to cite my reasons and strongly recommended that a significant amount of training be devoted to computing. Two of the four discussants (Professor Greenberg, Univ., N.C. and Greenhouse, F.W.) disagreed with my view. Later, Professor Chin Long Chiang of Berkley published an article disagreeing with my view on computing.

It is now 18 years later! I still hold the same view on the role of computing—not only in biostatistical science, but in statistical science. At that time, I had described the history of development of statistical software in four stages. The final stage referred to as stage IV described automatic data analysis systems. By this term I meant that the user will input a set of "stylized" questions dealing with various hypotheses or models. The system will automatically choose one or more appropriate statistical techniques and give the answers to the stylized questions. Also, the computer will indicate various caveats or cautions relating to possible shortcomings of the methodology—for example, concerning assumptions, robustness or approximations—and how they might affect the conclusions. I predicted this stage would arrive in about a decade. It has been almost two decades now and the computer has yet to assume the role of an intelligent data analyst.[1]

One of the problems we are experiencing in computing is that the cost of software seems to be climbing. In former times we were accustomed to having available whatever software was required, as cost was a relatively negligible item. However, this is no longer true today. I know of one software system for clinical trials that costs over $50,000. Routine general-purpose statistical software is costing more than $1,000. I believe this system may change by having statistical software on the Internet. The user will not have software resident on the user's computer. However, with a password, he or she will be able to use the software and payment will be made by amount of use. It is expensive to write good software. These software developers should be fairly compensated. However, a system has to evolve that prevents use of the software because of costs.

I now wish to conclude my talk by speaking directly about the future. I must confess to some apprehension about discussing the future. One need only pretend that it is 100 years ago and one is predicting the future of statistics. At the turn of the 20th century, there was a serious debate whether statistics was a separate discipline or part of sociology. There was a schism between

political arithmetic and those who attempted to simply gather data. Summary tables were considered a major advance in England. Galton had founded the science of eugenics. Karl Pearson was Galton's successor in this endeavor. Today, there work would be labeled as racist. In France and Russia, there was a tradition of research in probability, whereas in Germany and Italy, statistics was regarded as the practice of political arithmetic. No sooth-sayer could have even come close to predicting how statistics would develop over the next century. My view of the future is confined only to the next decade.

I believe that the demand for statistical scientists will continue to accelerate. Furthermore, we will not be able to come even close to fulfilling the demand. We will find large numbers of computer scientists and individuals trained in non-statistical disciplines to be fulfilling the role of data analysts. So called "data mining techniques" will be widely used on large databases. There is an urgent need for individuals to be able to extract information from data.

The demand for biostatistical scientists will continue unabated. Clinical Trials will continue to be a major activity. However, the field of Molecular Biology is turning into a field of Information Technology. Not too long ago, one would have a hundred bench scientists generating new data and only a handful of individuals analyzing the data. We now are in the reverse situation. A handful of bench scientist can generate an enormous amount of data that will require hundreds of data analysts. The availability of large molecular databases and the decoding of the human genome will allow scientist to plan an experiment and immediately obtain the data from the database. This is an activity in which statistical scientists can excel. The use of micro-array technology has created novel statistical problems, which are begging for statistical input.

I believe that financial institutions will be employing statistical scientists in ever-growing numbers. Wall Street firms are already hiring statistical scientists to work on options and derivatives. Credit card companies are amassing huge databases that need proper analyses. The same is true with any business or industry in which databases are important. The analysis of large databases will be a major pre-occupation of many Statistical Scientists.

As mentioned earlier, I believe there will be major efforts in the Pacific Rim countries in the area of Biostatistical Science. It would not be surprising to see the leadership in Biostatistics held by the U.S. to begin to move to the Pacific Rim countries.

I think that the Universities and Industry—especially the pharmaceutical industry will be forging closer relations with each other. Many of their major goals are shared and it is timely for industry to aid and participate in the educational process. There is a growing trend towards less NIH and more industry support for clinical trials. It is in the best interest of industry to forge close ties with universities.

Universities are relatively conservative institutions. They are slow to change. Science and technology are moving at a very fact pace in the developing countries. Somehow we in the Universities must keep up and be able to change curriculum and goals to meet emerging national needs and priorities and the new scientific opportunities.

Finally, I wish to remark on the role of statistical science on policy issues. We have much to contribute to policy. I would urge our profession to regard this as a major goal for the future. Many policy decisions are based on quantitative information. It is timely for our profession to expand our role as not only being responsible for the collection and interpretation of data, but to also take leadership in making policy.

I hope to be invited back to the ICSA in about a decade from now to assess my future predictions.

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1. Keynote talk presented before the International Chinese Statistical Association's 2000 applied Statistics Symposium, Piscataway, N.J., June 3, 2000

- Thinking has its place ..., but only when one is confronted with known facts and statistics. When you're in the unknown and the dark ..., you surrender your thinking in trust to the feelings that come to you out of the bush.

  "A Far-off Place" by
  Laurens Van Der Post (Penguin, 1976; p.248).

- Variance is what any two statisticians are at.

- To understand God's thoughts we must study statistics, for these are the measure of his purpose.

  Francis Nightingale

- "Statistics is a body of methods and theory that is applied to numerical evidence when making inferences in the face of uncertainty".
  Laurence Lapin in Statistics: Meaning and Method, 1980,

DR. PEI-CHING TANG (唐培經) (1903 – 1988)

A Memoir by his son and daughter

Yi-Ping Tang & Helen Tang Bhattacharyya, Pfizer Inc.

HIS EARLY EDUCATION

Dr. Pei-Ching Tang was born in a small village in the County of Chingtan (金壇), Kiangsu (江蘇) Province, China on April 30, 1903. It was a time when children born in rural areas seldom received any education, but his father insisted on sending him to schools, even to the extent of putting the family in debt.

His first schooling was in an old-style classroom studying classical Chinese. After the 1911 revolution overthrowing the Ch'ing Dynasty, he entered a newly founded public school, and later his father sent him to better schools in Wushi and Nanking. Graduating with top honors from high school, he was accepted into Southeast University in Nanking without entrance exam and obtained his BS in Mathematics in 1927.

He taught mathematics in middle schools after graduation. Anxious to continue his studies, he readily accepted when Tsing Hua University offered him a lecturer's position in the Mathematics Department in 1929. He was married then and moved his family to Peiping (Beijing).

China under the Ch'ing dynasty went through a series of disastrous foreign invasions during late 1800's, each resulting in concessions and payment of war reparations. The largest reparation was in 1900 when an allied force from eight countries invaded China during the Boxer rebellion. Part of the reparation, known as the remitted Boxer indemnities (庚子賠款), eventually was made available for Chinese nationals to study abroad. Tang was awarded such a grant in 1934 following fierce competition while teaching and continuing his studies at Tsing Hua University.

HIS STUDY IN ENGLAND

The early 1930s were a period of broad-based development and modernization in China. Statistics was being introduced to policy decisions, and seeing the importance of central planning, Tang chose to pursue his studies in mathematical statistics. He began his studies in statistics at the University College London in 1934. Karl Pearson had just retired in 1933 and the department was being split into the Department of Eugenics headed by R. A. Fisher and the Department of Statistics headed by Egon S. Pearson. This was a period of creative ferment in statistics and University College London was at the center of it. Jerzy Neyman was working with E.S. Pearson in formulating the theoretical framework for constructing most powerful statistical tests and laying the foundation for what is now regarded as "classical" statistical inference. Fellow Chinese students included P. L. Hsu (XU Bao Lu 許寶騄, ICSABulletin, July 2000, p.14-17), also from Tsing Hua.

Tang studied with Professor Pearson and worked on the sampling distribution of analysis of variance test, later known as the non-central F distribution, and showed its applications in determining sample sizes satisfying prescribed size and power for specific alternative hypotheses. With hand-cranked calculators of the time, Tang computed the tables, later known as Tang's tables. These tables have been useful to generations of statisticians who needed to calculate appropriate sample sizes for analysis of variance and other tests based on the F distribution (Statistical Research Memoirs, University College, London, Vol. 2, 128-149, 1938). Tang was awarded the degree of Ph.D. in Statistics in May 1937 and was admitted to the Royal Statistical Society as a Fellow. His wife, Yoong Wong (汪沅) Tang, who joined him in 1935 also studying statistics at University College, was awarded a M.S. degree.

HIS CONTRIBUTION IN CHINA

The Japanese attacked China at Marco Polo Bridge (盧溝橋) near Peiping in July 1937 and plunged China into a war that lasted eight years. Dr. and Mrs. Tang returned to China to be part of the national resistance effort. He accepted a teaching position at the National Central University and moved his family with the university to Chungking, the war-time capital of China. He taught mathematics and statistics at National Central University and wrote textbooks on statistics. Under the extreme conditions of the time, there was not the environment to do research but he was recognized for his management skills and was asked to be the Director of Freshmen Campus and later the Dean of National Central University. Mrs. Tang taught at Chungking University during this time. World War II ended with Japanese surrender in 1945 and National Central University moved back to Nanking. Tang continued teaching and, broadening his interest in education and national planning, was eventually named Director of Higher Education in the Ministry of Education in 1948. However, another tidal wave was sweeping across China in 1949 with the establishment of the People's Republic of China.

HIS CAREER AFTER LEAVING CHINA

During the years after Second World War, Tang had opportunities to meet and become friends with W. Edwards Deming and C. F. Taueber, who were instrumental in helping Tang pursue a career abroad. He was offered a Rockefeller Foundation grant in 1949 for agriculture research in the United States, followed by a United Nations Food and Agricultural Organization (FAO) assignment to teach sampling methods at a training center in Costa Rica. This was an exciting time in Costa Rica. After the end of a civil war and the founding of the Second Republic in 1948, Costa Rica was heavily investing in nation building with help from the United States and international organizations. Massive social and economic changes were taking place, such as voting rights for women, full citizenship for blacks, abolition of the armed forces, and focus on data gathering including broad based agriculture census for national planning purposes. After the initial short assignment in Costa Rica, Tang was asked by FAO later for more extended assignments there and eventually throughout Latin America.

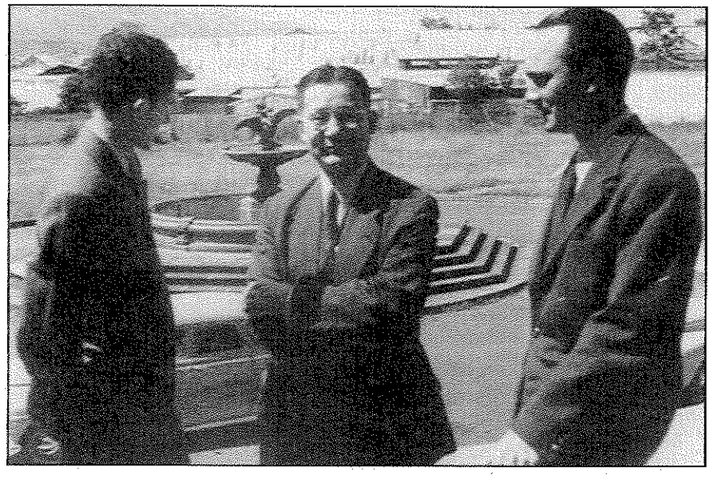
Before his long term assignment with FAO in 1952, Tang spent a year as visiting associate professor at Iowa State University in Ames, Iowa, where he had been visiting faculty in 1947, teaching sampling theory. In recognition of his contributions to the field of statistics, he was elected a Fellow of the American Statistics Association in 1952, being the first Chinese so honored. The citation read in part, " … for his tables and other statistical researches in the testing of hypotheses, which have led to world-wide recognition."

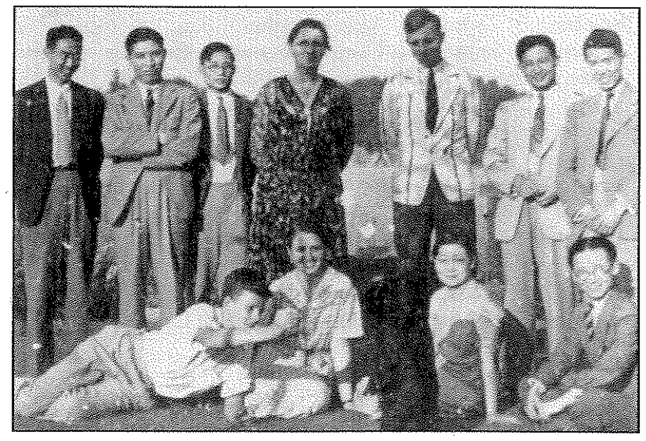
During Tang's years with FAO, from 1952 until his retirement in 1968, he traveled widely throughout Central and South America. He made his home in Quito, Ecuador; then

in Lima, Peru; and eventually in Santiago, Chile in 1960 when he was appointed the Regional Statistician for Latin American Countries. There he had the responsibility for planning and consulting on FAO statistical activities for all Latin America. During those years, as throughout his life, Tang emphasized the importance of education and was helpful in particular in guiding candidates in pursuing careers in statistics. After retirement, Tang settled in Washington D.C. where he had many friends. There he continued to work for two more years in training programs sponsored jointly by FAO and USDA for agriculture statisticians from all over the world.

Dr. Tang's first wife, Yoong Wong, died in 1971. They had two sons and two daughters. He married Beatrice Hu (胡佩英), an architect in Washington D.C., in 1973. His old age was not luxury but comfortable, surrounded by friends and family. Dr. Tang died in 1988 at the age of 86.

Photo 1: January 15, 1951
Photo 2: in London





SPECIAL TOPIC

FINANCE

Some Statistics Used in Finance

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Uncertainty plays an important role in both financial theory and empirical study. Random fluctuations require the use of statistical methods for testing the models obtained. Time series, multivariate analysis and Bayesian methods are statistical tools frequently used in academic finance literature.

The random walk hypothesis is a necessary condition for efficient asset market. Many testing statistics are used for different versions such as runs, Box and Pierce Q_n, Q_n' and variance ratio [1]. The unit root test is also related to the random walk hypothesis. The Dickey-Fuller test is used for the time series with a drift term in the absence of serial correlation and Phillips-Perron test is used for time series with serially correlated disturbance [2]. The R/S statistic (rescaled range statistic) is suggested to detect long range dependence in economic time series by using the fractional Brownian motions [1].

Testing the null hypothesis of co-integration is another statistical research problem related to time series analysis. Maximum likelihood estimations and a likelihood ratio test can be found in [2]. There is also a test for testing the null hypothesis of exactly h co-integrating relations. Johansen (1988) showed that the asymptotic distribution of the likelihood ratio is the same as that of the trace of matrix with integrals of the Brownian motion [2].

Volatility with auto-regression conditional heteroscedasticity is another subject in time series. ARCH, GARCH and EGARCH models often appear in the analysis of finance data. It can work better for the local time structure with different distribution families. Stochastic auto-regressive volatility is the natural generalization of ARCH model [3]. From the statistical theory, we can control the test level α, where α is the probability level we reject the hypothesis when it is actually true. However we can't control the probability of type I error, i.e. we accept the hypothesis when it is actually wrong. Many empirical study literatures use the statistical test in this way: they like to accept the hypothesis then get the following conclusions. The market is efficient, there is a unit root, there are h co-integration relations and it may be used in a wrong way.

Credit comes from a wide variety of sources, especially in finance. Some examples are credit cards, bank loans, car finance schemes and so on. Credit scoring and credit adjustments are the typical techniques for using the multivariate

analysis method. Classification and discriminate analysis [4] are the primary methods. With training samples, we can classify the sample into two groups: those which will be accepted and those which must be rejected. Among the accepted group, each person can get a score of credit according to the information on his family, occupation, banking relationships, income and expenditure... etc. Regression, logistic regression and probit analysis are also used to get the credit score. RPA (recursive partitioning algorithm), developed by Breiman et al. (1984) [5], is a classification tree approach. Boyle et al. (1994) [4] compares the RPA with discriminate analysis and suggests that RPA is a competitive approach. The other statistical method is to use the nearest neighbour ideas to classify the new applicants.

Bayesian analysis of time series has a long history. Moreover, there are some new methods developed by Zellner and Min who provide many successful applications in economic time series [6]. BMOM (Bayesian method of moments) and turning point prediction are the typical examples. BMOM only depends on some simple assumptions. Then, by the Maxine density (maximum entropy density function with specified moments), it is easy to get the posterior density and make the prediction. Linear model plays an essential role in all these approaches. A time series with finite observation data is also a linear model. The advantages of BMOM method is that we can find the turning point only by comparing the posterior probability and can do better with loss functions.

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Statistics and Futures Markets

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Statistics plays an important role in futures market research. In order to help statisticians understand the use of statistics in futures markets, we will first describe what is a futures contract and the economic functions of futures market. Building on this background, we will briefly discuss the motivations for the use of various statistical methods in several research areas of futures markets.

I. What is a futures contract ?

A futures (or forward) contract is an agreement to buy and sell in the future a specific quantity and a specific grade of underlying asset at a specific price. At the time of maturity, a futures contract is settled either by physical delivery or by cash settlement. The major economic functions of futures market are: (1) to provide market participants a low cost means of transferring price risk and (2) to provide price discovery function for the market participants (i.e. hedgers, speculators and arbitrageurs).

II. The use of Statistics in Futures Markets

Research in futures markets is often related to the examination of economic performance of futures markets and to the improvement of trading techniques for the market participants. Several selected research areas of futures markets are described as follows:

(1) Stochastic Models for Futures and Cash Market Prices

Stochastic models (data generating process) for futures and underlying cash price are required inputs for the Pricing futures and option on futures contracts, testing efficient market hypothesis and estimation of optimal futures hedging positions for hedgers to eliminate their price risk. Inter-temporal relationships among futures and cash prices are often examined in order to estimate market linkage between futures and cash markets and the feasibility of speculative spread trading. Statistical methods such as Probability distribution models, Linear and nonlinear time series, Monte Carlo simulation and Stochastic processes are often used in these areas.

(2) Risk Premium and Evaluation of Futures Prices is an Unbiased Predicator of Future Spot Price.

Futures prices at the time t are often used as useful predictor of expected future spot price in t+ τ period ahead. There is considerable controversy whether futures price is an unbiased predictor due to the possibility of the existence risk premium in futures prices. Co-integration analysis is often used in this topic of investigation.

(3) Margin Requirements and Cash Settlement Indices

A margin on a futures contract is a good –faith deposit to guarantee that holders of futures contract will perform their contractual obligation. A portfolio margin requirement established by Exchanges depends on the inputs of volatility and correlation of futures prices and distribution assumptions of futures prices. Thus, nonlinear time series models for time-varying volatility and correlation are often used in this area. Recently, statistical analysis of extreme value events has been used in stress test for intra-day margin requirements.

Futures contracts are often settled in cash rather than physical delivery. When there are several local cash delivery markets, multivariate statistical methods are also often employed to construct a composite cash index based on price inputs from these local cash markets

(4) Market Microstructure of Futures Markets

In general, market microstructure deal with the following topics: (a) price formation and price discovery; (b) information and disclosure, especially market transparency (the ability of market participants to observe information about the trading process); (c) liquidity and relationships between markets. Empirical studies in these areas often employed high frequency data (intra-day data or trade by trade transaction data) to verify the implications from theoretical models and to evaluate market performance. The statistical methods used in these topics often include state space models to estimate unobserved components (for example, true equilibrium

price and bid ask spreads) of price generating process and the application of point process technique to analyze irregular space trade by trade data (see Engle (2000)).

In summary, linear and nonlinear time series, linear models, multivariate analysis and stochastic processes are often used in the empirical analysis of futures market research. I recommend readers to read the paper by Lo (2000) and Handbook of Statistics 14 edited by Maddala an Rao (1996) for further discussion on the application of statistics in finance.

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Statistical Modeling of Stochastic Volatility in Financial Markets

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It is well accepted by researchers in statistics, finance and economics that volatility in financial markets changes over time. Engle (1982), Bollerslev (1986), Nelson (1991) and other researchers proposed various ARCH models for changing volatility. An alternative method, which has attracted much attention recently, is the stochastic volatility (SV) modeling. A discrete time version of the SV model given in Taylor (1982, 1986) is

$$r_t = \exp(h_t/2)u_t ,$$
$$h_t - \mu = \phi(h_{t-1} - \mu) + \eta_t ,$$

where r_t is the mean is the mean-correlated return of a financial security. We assume that the zero-mean white noise u_t and η_t are stochastically independent with variance one and σ^2 respectively. The above SV model can be transformed into a state space model by considering $y_t = \log r_t^2$. The measurement equation is given by

$$y_t = h_t + \xi_t ,$$

where $\xi_t = \log u_t^2$ is distributed as $\log \chi_1^2$. Accompanied with the state transition equation, the SV model can be viewed as a non-Gaussian state space model. Performing maximum likelihood inference for the SV model is much harder than ARCH models because the likelihood function of a non-Gaussian state space model is analytically intractable. Differing from the Gaussian state space model likelihood which can be evaluated with one pass of Kalman filter, the likelihood of the SV model using numerical methods like that in Kitagawa (1987) can be very time consuming. Without recognizing the SV model as a state space model, Taylor (1982, 1986) used the generalized method of moments type of estimators for the unknown parameters μ, ϕ and σ^2. Harvey, Ruiz and Shephard (1994) gave an attempt to obtain the parameter estimates under a state space form. They proposed the quasi-ML approach by regarding ξ_t as a normal random variable.

The recent advance of statistical computing technology allows us to tackle the inference problem in both frequentist and Bayesian perspectives. Shephard (1993) and Jacquier, Polson and Rossi (1994) proposed the simulation-based approach by sampling the parameters and the latent variables h_t from their joint posterior distribution via Markov chain Monte Carlo methods. Since then, with various modifications of these Bayesian methods (Shephard 1994, Shephard and Pitt 1997, Kim, Shephard and Chib 1998), posterior inference of the SV model can now be carried out efficiently. Another Monte Carlo sampling approach is the simulated ML method suggested in Danielsson (1994). A far more efficient version based on importance sampling, which is also applicable to general non-Gaussian state space models, was investigated in Sandmann and Koopman (1998).

Since the above basic formulation of the SV model is not adequate to capture all the stylized facts of financial returns, many extensions have been considered. Jacquier, Polson and Rossi (1994a) and Chib, Nardari and Shephard (1998) assumed a fat-tailed distribution for u_t. Harvey and Shephard (1996) used correlated u_t and η_t to explain the well-known leverage effect in stock returns. So, Lam and Li (1998) introduced the Markov Switching SV model to allow volatility to switch between different regimes. Harvey (1993) and Breidt, Crato and de Lima (1998) proposed the long memory SV model to explain the long-range dependence in volatility. Besides the univariate modeling, Harvey, Ruiz and Shephard (1994), So, Li and Lam (1997) and Pitt and Shephard (1999) investigated multivariate SV models in which latent factors can also be incorporated in the models for more parsimonious fitting.

In summary, more advanced statistical inference techniques for SV models under the state space setting are expected. In the financial perspective, market practitioners and financial analysts may want to see more evidence in supporting the use of SV models as an alternative to ARCH models.

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Statistics Application in Finance

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GMAC-RFC (Residential Funding Corporation), headquartered in Minneapolis, was founded in 1982 as an issuer of securities collateralized by non-conforming "A" product, making it the oldest private label mortgage conduit. Since its inception, GMAC-RFC has issued more than $100 billion of public securities. GMAC-RFC is a wholly owned, indirect subsidiary of General Motors Acceptance Corp. (GMAC), which acquired RFC in 1990. Today, GMAC-RFC and its subsidiaries and affiliates have a presence in several industry segments, including:

- Warehousing lending.
- Construction lending.
- Commercial (multifamily) lending.
- Portfolio acquisitions (seasoned, subprime, and non-performing).
- Direct origination.
- International mortgage finance and servicing (Japan, U.K. and Latin America).
- Residential mortgage servicing (master, primary, and special servicing).
- Real estate owned (REO) management and disposition.
- Broker-dealer.
- Distressed credit card receivables.

As the largest private residential mortgage conduit, GMAC-RFC's loan acquisition programs include a broad mix of products. GMAC-RFC acquires mortgages from a variety of sources, with each having specific needs and requiring specific expertise. Therefore, several different business units, each of which specializes in a certain type of origination client, handle the company's acquisition efforts. Together, these divisions provide a wide array of loan programs, including first mortgages, home equity, subprime first mortgage, and high loan-to-value (LTV) products. This specialization has been implemented to facilitate the acquisition of better-quality loans through improved client relationships and risk management practices, as well as the application of more consistent underwriting standards.

GMAC-RFC distributes its products through Wall Street dealers and directly through its two broker-dealer subsidiaries, Residential Funding Securities Corp. (RFSC), a National Association of Securities Dealers registered broker-dealer, and RFSC's U.K. affiliate, Residential Funding Securities Corporation International Ltd. (RFSCIL). GMAC-RFC is a leader in mortgage- and asset-backed securitization through core expertise in:

- Securitization: GMAC-RFC's domestic loan programs fall under five primary groupings – jumbo "A", expanded criteria, home equity, AlterNet, and portfolio transactions. GMAC-RFC securitizes these products through four separate and distinct shelves. Each shelf is structured to provide a distribution channel tailored to match GMAC-RFC loan products to the varied risk-characteristics demanded by investors.
- Lending: GMAC-RFC (1) offers a diversified array of lending and depository products to residential and commercial mortgage banker nationwide; (2) offers standard construction loans, residential equity, special project needs, and working capital lines; (3) originates and acquires commercial mortgages, principally mortgages on multifamily, retail, office, and industrial properties through a national network of commercial mortgage bankers.
- Investment

GMAC-RFC engages a fully staffed Mortgage Credit Risk Management Department with a clear objective to monitor and manage risk, to provide sound relevant credit risk recommendations, to refine program policies and guidelines, and formulate credit policy. We do this by:

- Loan/portfolio performance monitoring – we monitor performance by loan characteristics and by seller.
- Model development and validation – we have created models for new origination and seasoned loans. Logistic regression and proportional hazard modelling techniques are applied. Mortgage Credit Risk Management has also reviewed and analyzed third party's models to provide GMAC-RFC originators flexibility in the underwriting process while still maintaining the highest standards of risk management. Cross-Tabulation, K-S statistic (Kolmogorov-Smirnov two-sample test), ROC curve (Receiver Operating Characteristic curve), and

Cost-Benefit analysis techniques are applied.

- Credit loss and reserve forecasting – we use our proprietary scoring models to calculate probability of default for new originated and seasoned loans. Reforecast adjustments are performed quarterly based on actual delinquency and prepayment performance.
- Regional economic and home price movement analysis by MSAs (Metropolitan Statistical Areas) – We forecast home price movements by time series analysis technique, and economic conditions in markets where GMAC-RFC is currently doing business, in order to provide insights and recommendations for strengthening out credit underwriting decisions and assessment of the underlying collateral value securing the loans we purchase.

Mortgage Credit Risk Management Department has developed forecasting and modelling tools to enable GMAC-RFC to make more informed purchase decisions. One tool that is integral in our origination process is the PAScore (Pre-funding Acquisition Score). PAScore is used in the origination of loans to:

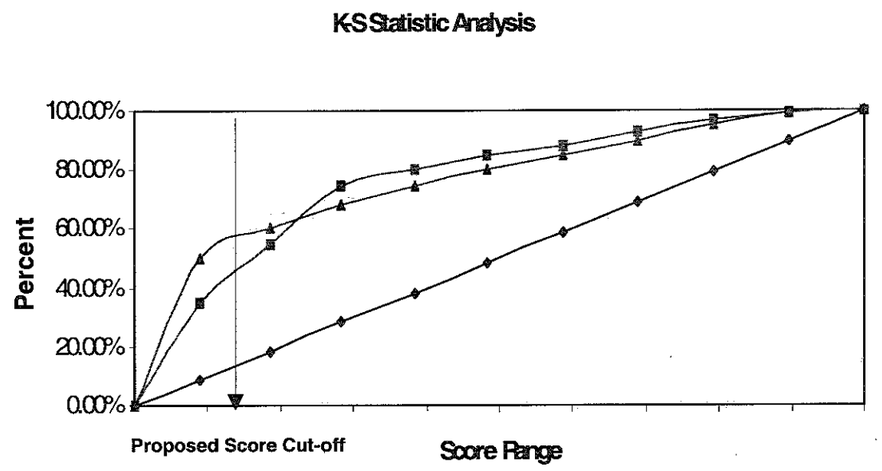
- Determine mortgage default risk; and
- Better quantify value of loans to buy/sell

Credit score, such as FICO (Fair, Isaacs) determine credit risk, or the probability that the borrower will default, using tradeline, payment history and outstanding debt from the borrower's credit report. Mortgage scores (the PAScore) determine the probability of default using the borrower's history and other loan characteristics proven to predict delinquency. The PAScore uses the FICO score as the credit component, and combines this with other loan characteristics, including (but not limited to):

- Home Price Movement
- Loan-to-value ratio (LTV)
- Debt-to-income ratio (DTI)
- Principal purchase balance
- Payment type (ARM or Fixed-Rate)
- Owner occupancy
- Prior mortgage history (foreclosure, late payments)

Credit and mortgage scores play an important role in a sound credit policy. However, these scores are only one component of an overall methodology for monitoring and controlling risk. Credit and mortgage scores only assist with the decision process and should not be used on an isolated basis. For this reason, GMAC-RFC maintains a common sense approach to underwriting with a willingness to entertain well-documented exceptions. Risk Management is an important component of GMAC-RFC's overall strategy to continue as a leading issue of mortgage- and asset-back securities. We believe strongly in supporting the securities we deliver to the market by creating and utilizing effective tools for monitoring and controlling risk.

In the following hypothetical example, a sample of GMAC-RFC loans originated over a defined period of time, consisting of "current" (Good) and "90+ days late payment" (Bad) were selected. Comparisons were made between two different scoring models. While the K-S statistic for Model 2 indicates superior separation at the point of maximum separation between goods and bads, further analysis must be done to ensure that Model 2 has better separation of goods and bads within the relevant score ranges. The following illustration shows the K-S statistic at the proposed score cut-off for Model 1 is greater than Model 2. K-S statistic measures the maximum separation between two cumulative density functions (the cumulative good curve and the cumulative bad curve). A comparison of models using this statistic can be very misleading since what matters is the K-S statistics at the score range where approve/decline or pricing decisions are made.



SPECIAL TOPIC

Note on Survey/Poll continued from July 2000

☛ A follow-up from the previous issue of special topic column "Survey/Poll": Presidential election of 2000 in US took place in November 7, 2000. However, the result could not be finalized until the Electoral Day of December 12, 2000. The contentious issue was mostly on criteria (specified before versus after the election) used to cast the ballots and statistical errors of margin in counting the ballots. Interested readers are referred to Weblink to US 2000 presidential election:

http://www.stats.org/newsletters/0010/checklist.htm
http://www.stats.org/newsletters/0010/predict.htm
http://www.stats.org/newsletters/0010/implementation.htm
http://www.stats.org/newsletters/0010/biblio.htm

Special thanks to Dr. Timothy Chen, our president of 1999, for providing these weblinks.

!!! Controversial !!!
Statistical
Issue

Active Controlled Clinical Trials

Non-Inferiority Trials: Does Sloppiness Bias Toward No Difference?

By Irving K. Hwang, Ph.D.
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"Assay Sensitivity," as defined in ICH E10 Guidance [1], is a property of a clinical trial that has the ability to distinguish an effective treatment from a less effective or ineffective treatment. In a superiority trial, when a test treatment is shown superior to the control (placebo or active control), the finding itself demonstrates assay sensitivity. However, in a trial intended to show a test treatment is non-inferior to an active control, assay sensitivity can only be deduced from historical evidence of sensitivity to drug effects of the chosen active control and appropriate trial conduct (high quality) of the current non-inferiority trial.

It is well understood that in a superiority trial with an intention to show difference between treatments, there is strong imperative to design and conduct the trial with good quality to increase the likelihood of demonstrating assay sensitivity. Whereas, in a trial intended to show no difference of a particular size (i.e., a non-inferiority margin) between treatments, there is a much weaker stimulus to optimize study design and reduce study errors due to the expectations of patients and investigators on receiving active treatments. It is generally believed that in a non-inferiority trial, trial sloppiness (poor trial quality) would bias toward no difference [2,3] and in turn, increase the likelihood that an ineffective treatment could be found non-inferior. Is this belief statistically plausible?

Prior to answering this question, it is necessary to compare the null and alternative hypotheses of the superiority trial with those of the non-inferiority trial. When the concept of hypothesis testing, or equivalently, the notion of confidence interval, is fully appreciated, the similarity between these two types of trials, as shown below, will become obvious.

Superiority Trial	**Non-Inferiority Trial**
$\mathbf{H_0}$ (no treatment difference): $\mu_t - \mu_c = 0$ vs. $\mathbf{H_1}$ (test treatment better): $\mu_t - \mu_c > 0$. To reject the null hypothesis (showing test treatment superior), it is necessary that $z = (\bar{x}_t - \bar{x}_c) / s_{(\bar{x}_t - \bar{x}_c)} > 1.96$.*	$\mathbf{H_0}$ (test treatment inferior): $\mu_t - \mu_c < -\delta$ vs. $\mathbf{H_1}$ (test treatment non-inferior): $\mu_t - \mu_c \geq -\delta$. To reject the null hypothesis (demonstrating test treatment non-inferior within the margin, δ), it is necessary that $z = ((\bar{x}_t - \bar{x}_c) + \delta) / s_{(\bar{x}_t - \bar{x}_c)} > 1.96$.*

* Assuming the test is one-sided at $\alpha = 0.025$ level with a critical value = 1.96. Where μ_t and μ_c represent the population means and $\bar{x}_t$ and $\bar{x}_c$ the observed (sample) means for the test and control treatments, respectively, $s_{(\bar{x}_t - \bar{x}_c)}$ represents the observed (sample) standard error of the mean difference, and $d = \bar{x}_t - \bar{x}_c$ such that $s_{(\bar{x}_t - \bar{x}_c)} = s_d$

In a superiority setting, it needs a large numerator (large observed mean difference, d), and/or a small denominator (small observed standard error of the mean difference, s_d), to make the test statistic significant ($z > 1.96$, $p < 0.025$), and thus show test treatment superior. Similarly, in non-inferiority setting, it also needs a large positive numerator, $(d + \delta)$, and/or concurrently a small denominator, s_d, to reach significance, and thus demonstrates test treatment non-inferior. In fact, good trial design and conduct with large observed differences and/or small standard errors are necessary regardless whether a trial is designed to show superiority or non-inferiority.

Now, let us examine whether trial sloppiness in a non-inferiority trial indeed biases toward no difference and in turn, increases the likelihood that an ineffective treatment could be found non-inferior. In fact, the test statistic for the non-inferiority trial is:

$$z = (d + \delta) / S_d$$

Reject $\mathbf{H_0}$: $\mu_t - \mu_c < -\delta$ to conclude non-inferiority of test to active control, if $z > 1.96$. Equivalently, one can use the confidence interval (CI) approach to claim non-inferiority, if, $[C_L, \infty)$, the 1-sided 97.5% CI for $\mu_t - \mu_c$, is included in $[-\delta, \infty)$ or $-\delta < C_L$, where C_L is the lower limit of the 1-sided 97.5% CI.

No difference means $d = 0$. Whether one can reject $\mathbf{H_0}$ and claim non-inferiority will depend on the relative magnitude of δ to s_d (i.e. the ratio of δ / s_d) when $d = 0$. If the ratio of δ / s_d is greater than 1.96, then one can reject $\mathbf{H_0}$ and claim non-inferiority. Otherwise, one would have to declare inferiority, since δ is the appropriately chosen non-inferiority margin which is usually small unless the standard error of d is much smaller. Therefore, no difference (i.e., $d = 0$) does not necessarily imply non-inferiority.

Sloppiness usually introduces noise. Noise implies increased variability with wider confidence interval and in turn it biases toward $\mathbf{H_0}$. In addition, sloppiness generally introduces bias. Bias may happen in either direction (i.e., reduced or increased observed difference, d). Therefore, sloppiness may bias toward either $\mathbf{H_0}$: $\mu_t - \mu_c < -\delta$ (inferiority) or $\mathbf{H_1}$: $\mu_t - \mu_c \geq -\delta$ (non-inferiority), though the latter is the major concern in conducting non-inferiority trials.

Discussions on this issue can also be found in Hwang & Morikawa [4] and Hauck & Anderson [5].

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Non-inferiority: A Dangerous Toy?*

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A clinical trial as an experiment on humans often needs to be run using a complex design for ethical reasons, that is, the welfare of patients in and out of the trial must be properly considered. As more or more effective treatments have been available to the patients, the clinical trial for studying the effectiveness of an experimental treatment, particularly in the same class of the effective medical products, can be very difficult to design. At least, use of placebo can be challenged. The only viable choice seems to be use of a positive control. A difficult task is choice of an effective treatment from the historical trial experiences to serve as a control for the experimental treatment to compare against in the positive control trial. If it can be shown more effective than the positive control, the new treatment is usually accepted as an effective treatment.

Problems arise when a greater effect with the new treatment may not be possible to show, perhaps because in truth the effect difference is minimal between the new treatment and the control. Under this scenario, the effectiveness of the new treatment will likely be established by arguing a minimal difference in the treatment effect or that the new treatment is minimally less effective than the control. The former is the concept of equivalence and the latter is non-inferiority, which is pursued more often than equivalence in therapeutic clinical trials. In the first place, there seems to be no problem with the non-inferiority setting. All needed is setting up a non-inferiority margin that is related to the acceptable degree of difference in treatment effect. It can be subjectively and arbitrarily defined. Certainly, such a way of selection causes a lot of concerns because of no reference to the position of the invisible placebo. So, recently, many scientists argue that choice of the non-inferiority margin should take into consideration the control effect, which is at best estimated from some historical trials. What a noble argument! It opens cans of worms. How should one do meta-analyses (or integrated analyses or pooled, combined,...) to estimate the control effect? By random-effect or fixed-effect modeling? Should we incorporate the error of the estimate in assessing the type I or II error probabilities incurring in non-inferiority statistical testing? Oh! No! this involves cross-study comparisons. In order to interpret the results of such comparisons, we require that both trial populations are randomly sampled from the same population (we know that random sampling is never in place) or well representative of the target population (we know that this is always not verifiable). Such comparisons are very problematic at least! In fact, talking about type I error probability for non-inferiority testing is wrong! But, we can calculate a p-value for comparing the new treatment with the invisible placebo and it is 10^{-16}. No! Posterior probability will work! Why isn't type I error an issue as it always is in any clinical experiment? We need a placebo arm but Hum! This is a moot point....

Let us take a step back. What is the non-inferiority hypothesis? For ease of presentation, let me use alphabetical letter to represent both a treatment group and its expectation of an interested response. Let T-C be the effect of the new treatment T relative to the concurrent positive control C. From the historical data, we have the parameters C_0 and P_0 of the intended-to-use positive control and the placebo, respectively. Originally, one possible null hypothesis for non-inferiority is H_0: $T\text{-}C \leq \delta$, where δ is the non-inferiority margin. This margin is only vaguely defined by referring to the estimated C_0 and P_0 at best. Thus, it does not make sense to write $\delta = f(C_0\text{-}P_0)$ for some function f because the essential questions of interest apply only to the current trial population. In addition, if this expression is sensible, then there is never a problem with statistical inference because the test statistic "carefully" constructed using approximately unbiased estimators for both sides of the inequality of H_0 will have an approximately correct type I error probability associated with this null hypothesis. Can δ be some function of C-P (P is the corresponding parameter of the invisible placebo that does not exist in the concurrent positive-control study)? This is exactly suggested by the essential questions of interest (the patients with the current disease conditions are of greater interest, not the historical patient population). Because of missing P, one may argue that the type I error probability is not computable. However, if one believes that C-P is estimable from the historical trials, then this hypothesis is testable. Moreover, one can assess the impact of the error in estimation of C-P using the estimate of $C_0\text{-}P_0$ on the error probability in testing H_0; see the reference [1].

Averaging is a well-known powerful tool in the human inventions. Let us take a simple average of C-P and $C_0\text{-}P_0$. The resulting average reflects the center of the

two centers. The deviations between the two centers and the resulting average describe heterogeneity between the centers. Imagine that there are many future positive control trials using the same positive control to develop new medicine. Continuous application of averaging will construct an interesting center and descriptor for heterogeneity between the centers, i.e., the parameters C-P from the historical trials and future positive control trials. This is, in essence, the basis of Bayesian framework. In some sense, such an averaging process updates the location of the control effect C-P from the past to the future. This concept is very natural. But wait a minute. There will never be any future data for C-P and the only data we have for C-P is from the estimates of C_0-P_0. While updating the location of C-P, the data remains at the estimates of C_0-P_0. So why will this framework have more advantage in terms of resolving the controversy?

In brief, we realized the controversy long time ago and got away from it for the most part. Now, we are part of the controversy in playing the dangerous toy – NON-INFERIORITY. Is it really that dangerous?

Reference

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Alternatives for Discounting Historical Data in the Analysis of Non-Inferiority Trials

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INTRODUCTION

Non-inferiority trials are clinical trials in which the goal is to demonstrate that the effect of an experimental treatment is not inferior to that of an active control by more than a specific margin. Often, a secondary goal is to indirectly compare the experimental treatment with placebo. The most common situation where this occurs is when the active control has been previously studied versus placebo, but including a placebo in a new trial would be considered unethical. In some cases this indirect evidence for an effect versus placebo has been used as evidence for regulatory approval of a new therapy.

The indirect comparison of the experimental treatment with placebo depends for its validity on two key assumptions: that the effect of the active control in the current trial is the same as it was in the historical placebo-controlled trials (constancy), and that the current trial has the same ability to distinguish the active control from placebo as the historical active-controlled trials (assay sensitivity). It is discomforting that these assumptions can not be directly verified within the current trial and that there are often reasons to doubt their truth.

These assumptions are discussed extensively in ICH E-10 guideline [1] and elsewhere [2-5]. Because of the questions surrounding the validity of the indirect comparison of the experimental treatment with placebo, it would seem reasonable to apply some type of discounting to the historical placebo-controlled data; that is, to give them less weight than if they were an integral part of the current trial. The purposes of this paper are to further discuss the concept of discounting, to show that various methods of analyzing non-inferiority trials can be put into the common context of discounting, and to compare the degree of discounting associated with these methods.

METHODS

Suppose the analysis variable of interest is binary, and that the method of analysis will be based on the log odds ratio, and that the summary results of the historical placebo-controlled trials and the results of the current trial are denoted as follows:

B_{SP}, V_{SP} the log odds ratio and its variance for the active control (standard) relative to placebo (from the historical trials).

B_{XS}, V_{XS} the log odds ratio and its variance for the experimental treatment to the active control (from the current trial).

If we can assume constancy and assay sensitivity and do not want to discount the historical data, then it is relatively simple to indirectly compare the experimental treatment to placebo, while fully accounting for random variation in the effects of all treatments. We simply sum the log odds ratios for the experimental treatment relative to the active control and for the active control relative to placebo to obtain an approximately normally distributed random variable with variance equal to sum of the two variance terms: $Z_0 \sim N(B_{XS} + B_{SP}, V_{XS} + V_{SP})$.

Discounting Approach #1: Setting a Non-Inferiority Margin

A frequent method of analyzing non-inferiority trials is to first specify a non-inferiority margin, denoted by δ, and then to compare the results of the current trial with that margin; if the confidence interval for the effect of the experimental treatment relative to the active control is entirely above this margin, then experimental treatment is declared non-inferior to the active control. In order to draw an indirect inference relative to placebo, the non-inferiority margin can be selected based on the historical placebo-controlled results. While it is not always recognized, this approach is extremely inefficient relative to the simple approach defined above, and therefore in effect includes a form of discounting.

Suppose, for example, that the non-inferiority margin is set to be the negative of the lower bound of the 2-sided 95% confidence interval for the effect of the active control relative to placebo in the historical trials, or $\delta = -(B_{SP} - 1.96\sqrt{V_{SP}})$, and that non-inferiority will be declared if the lower bound of the 2-sided 95% confidence interval for the effect of the experimental

treatment relative to the active control in the current trial is greater than δ, or $B_{XS} - 1.96\sqrt{V_{XS}} > \delta$.

This approach is essentially equivalent to indirectly comparing the experimental treatment to placebo using the following test statistic, in that a significant difference based on the test statistic corresponds to meeting the criterion involving the non-inferiority margin: $Z_1 \sim N\left(B_{XS} + B_{SP}, \left(\sqrt{V_{XS}} + \sqrt{V_{SP}}\right)^2\right)$

Note that Z_0 and Z_1 are similar, except that rather than pooling variances, Z_1 discounts by pooling standard errors.

Discounting Approach #2: Preserving a Fraction of the Active Control's Effect

The approaches described thus far are intended to indirectly compare the experimental treatment to placebo and to declare it effective if it has any benefit over placebo, regardless of the relative benefits of the experimental treatment and the active control. In some cases the goal involves a higher standard, at least on the surface: In order for an experimental treatment to be declared effective it must not only be superior to placebo, but also must preserve a specific fraction of the active control's effect relative to placebo. For example, in order to demonstrate preservation of half of the active control's effect, one must rule out an effect of the experimental treatment relative to placebo of less than ½B_{SP}.

There are two ways to view this requirement. On its surface, this is a new standard of effectiveness for the experimental treatment. This is somewhat controversial, since it is inconsistent with the usual standard for placebo-controlled trials. However, another less controversial viewpoint is that this is simply another means of discounting the historical data. In this view, a positive result would not necessarily mean that the experimental treatment preserves any specific portion of the active control's effect, but it would give greater confidence that the experimental treatment is superior to placebo.

While there are more sophisticated approaches that could be used [8], a very simple statistic that illustrates the discounting associated with preservation of 50% of the active control's effect is as follows: $Z_2 \sim N(B_{XS} + \frac{1}{2} B_{SP}, V_{XS} + \frac{1}{4} V_{SP})$

Discounting Approach #3: Double-Discounting

The final approach discussed here is referred to as the double-discounting approach, and has been proposed by the FDA in at least one clinical setting [9]. In this approach one applies the preservation of 50% of the active control's effect to the non-inferiority margin, or $\delta = -\frac{1}{2}\left(B_{SP} - 1.96\sqrt{V_{SP}}\right)$

This approach combines the discounting associated with setting a non-inferiority margin with the discounting associated with preservation of 50% of the active control's effect. Using the same format as before, a simple test statistic associated with this approach is given here: $Z_3 \sim N\left(B_{XS} + \frac{1}{2}B_{SP}, \left(\sqrt{V_{XS}} + \sqrt{\frac{1}{4}V_{SP}}\right)^2\right)$

A COMPARISON OF APPROACHES

Table 1 compares the statistics produced by Z_0, Z_1, Z_2 and Z_3 for various combinations of B_{SP}, B_{XS}, V_{SP} and V_{XS}. All else held constant, all statistics increased, indicating increasing evidence that the experimental treatment is superior to placebo, as either the strength of evidence that the active control is superior to placebo increased (*i.e.*, as B_{SP} increased for a fixed V_{SP}), or as the strength of evidence that the experimental treatment is superior to the active control increased (*i.e.*, as B_{XS} increased for a fixed V_{XS}). In all situations studied the statistics produced by Z_1, Z_2 and Z_3 were smaller than the statistic produced by Z_0, and the statistic produced by Z_3 was as small as or smaller than all others. Z_1 tended to be larger than Z_2, but not uniformly. The factors that tended to increase Z_2 relative to Z_1 were a relatively small level of evidence that the active control is superior to placebo and a relatively large level of evidence that the experimental treatment is superior to the active control.

Note that the degree of discounting produced by these statistics was sometimes fairly extreme. Take as an example the next-to-last row of the table. The statistic produced by Z_0 was 3.578, which corresponds to a highly significant 2-sided p-value of 0.0003, while the p-values corresponding to Z_1, Z_2 and Z_3, respectively, were 0.0077, 0.0524 and 0.1096.

CONCLUSIONS

It is clearly appropriate to discount the historical placebo-controlled data to some degree when indirectly comparing an experimental treatment to placebo following a non-inferiority trial, due to the uncertainty surrounding the assumptions that form the basis for the validity of that comparison. However, the level of discounting required is less clear since it is somewhat subjective and may be different in different situations. As described in this paper, finding the right level of discounting may be complicated by a lack of recognition of the sources of discounting associated with common methods of analysis of non-inferiority trials. It could be argued that we do not yet have a logical and consistent approach for discounting, and it may turn out that neither specification of a non-inferiority margin nor preservation of a fraction of the active control's effect will be the preferred method of discounting in the future. For example, applying a multiplicative constant to the variance for the effect of the active control relative to placebo from the historical trials has a logical appeal and may turn out to be the method of choice. Hopefully, the conceptual framework described here will be helpful in approaching this problem.

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Table 1
Statistics Produced by Z_0, Z_1, Z_2 and Z_3 for Various Combinations of B_{SP}, B_{XS}, V_{SP} and V_{XS}

B_{SP}	B_{XS}	V_{SP}	V_{XS}	Z_0	Z_1	Z_2	Z_3
2	-1	1	1	0.707	0.500	0.000	0.000
2	0	1	1	1.414	1.000	0.894	0.667
2	1	1	1	2.121	1.500	1.789	1.333
4	-1	1	1	2.121	1.500	0.894	0.667
4	0	1	1	2.828	2.000	1.789	1.333
4	1	1	1	3.536	2.500	2.683	2.000
2	-1	½	1	0.816	0.586	0.000	0.000
2	0	½	1	1.633	1.172	0.943	0.739
2	1	½	1	2.449	1.757	1.886	1.478
4	-1	½	1	2.449	1.757	0.943	0.739
4	0	½	1	3.266	2.343	1.886	1.478
4	1	½	1	4.082	2.929	2.828	2.216
2	-1	¼	1	0.894	0.667	0.000	0.000
2	0	¼	1	1.789	1.333	0.970	0.800
2	1	¼	1	2.683	2.000	1.940	1.600
4	-1	¼	1	2.683	2.000	0.970	0.800
4	0	¼	1	3.578	2.667	1.940	1.600
4	1	¼	1	4.472	3.333	2.910	2.400

Equivalence studies can not be used to claim equivalence of two active treatments

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In the ICH guidelines on Choice of Control Group and Related Issues in Clinical Trials (1), the concepts "equivalence trial" and "non-inferiority trial" are used to denote a clinical trial designed to demonstrate efficacy of a new drug by showing that it is similar in efficacy to a standard agent. As discussed in the guidelines, equivalence trials and non-inferiority trials may be an alternative to placebo controlled trials for showing efficacy of a new drug. The names "equivalence" and "non-inferiority" however indicate that these trials could be used for far stronger claims than efficacy, namely to claim that a new treatment is "as effective as" (equivalent to) or "at least as effective as" (non-inferior to) a comparator treatment. We want to argue that such use of equivalence and non-inferiority trials is incorrect, and we propose an alternative way to address the question of therapeutic equivalence.

To illustrate the problems we will consider the following example. Assume that we want to prove that 200 µg of the glucocorticosteroid A has the same clinical effect on asthma as 400 µg of the glucocorticosteroid B. To use a therapeutic equivalence trial, we first need to pre-define our equivalence limits. One suggestion for this (2) is that the mean difference in morning Peak Expiratory Flow should be within –15 to 15 L/min (i.e. a 95% confidence interval for the mean difference should be entirely within this interval). If we run a trial and get the 95% confidence interval -14 to 12 L/min, for example, can we then draw the conclusion that the two treatments are equivalent?

As a statistical procedure, the approach can be regarded as valid and the conclusion of equivalence is correct. From a medical point of view we would argue that the approach can be criticized and that the conclusion is not always correct. The first objection regards the pre-defined equivalence limits. If it is generally accepted that a mean difference less than 15 L/min is clinically irrelevant, there is no problem, but if there is disagreement about this, the conclusion of equivalence must be questioned. Anyone believing that smaller mean differences than 15 L/min are clinically important have the right to argue that the study is inconclusive. The fact that the equivalence limits are pre-specified does not make them generally accepted. Our first conclusion is therefore that the pre-specification of equivalence limits does not add any value to an equivalence study. The important result should be the actual confidence limits obtained in the study – the clinical interpretation of these are then what decides whether one could consider the difference small enough to be clinically irrelevant.
Our second objection regards the ability of the study to detect possible differences between the treatments. The ICH guideline clearly states that for an equivalence or non-inferiority trial to be valid, it must be supported with evidence that the trial had ability to distinguish an effective treatment from a less effective or ineffective treatment (so called assay sensitivity). This is even more important for a study aiming to conclude equivalence of two active treatments. In the example above, assume that we instead compared 200 and 400 µg of the same steroid. If we then got a confidence interval contained within the equivalence limits, should we then conclude that these two doses of the steroid are equivalent? If we accept the equivalence limits, it is probably correct that for these patients there is, on average, no point in increasing the dose. This does however not necessarily apply to a different patient population and generalization of the conclusion to a wider population than the actual study population is probably incorrect.
The same objection applies to the study comparing 200 µg of steroid A with 400 µg of steroid B. The strongest conclusion we should be allowed to make is that in the actual study population, the treatments produce on average the same result. Many observers would unfortunately draw one further conclusion – that steroid A is twice as potent as steroid B. This conclusion can not be drawn since there is nothing in the results to show that not also 200 and 400 µg of steroid A would have been considered

therapeutically equivalent in this study population. To conclude that there is a difference in potency there must be evidence that the study had ability to distinguish between different doses of the steroids.

Based on our two objections we suggest a different approach to therapeutic equivalence, and in fact, that the concept of therapeutic equivalence is not needed at all.
The approach we suggest is restricted to the situation when we have two treatments that can be given in different doses (the doses do not have to be approved or marketed). We then suggest a study where two doses of treatment A are compared to one dose of treatment B. We need to choose our patients and design the study so that we can statistically demonstrate a difference between the two doses of treatment A. In our previous example, we choose 100 and 400 μg of steroid A and 200 μg of steroid B. If the two doses of steroid A differ statistically significantly we approximate the dose response curve for steroid A with a linear function of log-dose. From this approximation we estimate the dose of steroid A corresponding to 200 μg of steroid B and calculate a confidence interval for the estimate (2,3). Assume that we get the estimate 186 μg with confidence interval 120 to 270 μg. If we are content with working with dose doubling steps, the interpretation could be that 200 μg of steroid A is therapeutically equivalent with 400 μg of steroid B. The argument would be that half the dose of steroid A, 100 μg, is too low and twice the dose, 400 μg, is too high.

If we are not content with working only with dose doubling steps, more specific equivalence limits must be agreed upon. The fact that we now work on the dose scale may simplify this. We would however argue that the important result still is the confidence interval for the dose of steroid A corresponding to 200 μg of steroid B and, in fact, that there is no need for a definition of therapeutic equivalence. By providing the estimate for the equivalent dose and confidence limits for this, it should be possible for the reader to assess to what extent this means therapeutic equivalence in practical terms. Whether the reader is the doctor, contemplating switching treatment for his patients, or the regulatory reviewer who must assess whether or not the evidence submitted is sufficient for a specific claim, the information should be sufficient for a decision to be made.

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Placebo Control, Historical Control and Active Control Trials*

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In order to demonstrate that a test treatment is effective, one needs to conduct a clinical trial to test for

$$H_0: T = R \text{ versus}$$
$$H_A: T > R,$$

where R is the reference treatment used as control. The test treatment is shown to be effective when H_0 is rejected (often required at α=0.025 level). The most common design for confirmatory clinical trials is the parallel group design. Based on the

different types of reference used in testing the null hypothesis, the parallel-group trial may be described as a placebo control, a non-treatment control, a historical control or an active control trial. In this article, we will examine the statistical properties of placebo-control, historical-control and active-control clinical trials for the testing of the null hypothesis. For simplicity and without loss of generality, we will focus on trials with no more than two different treatment arms.

I. Placebo-Controlled Clinical Trial

For treating diseases or symptoms with a non-negligible placebo effect, placebo is often selected as the reference treatment. Let P denote the true response value of the placebo group, then the hypotheses are

$$H_0: T = P \text{ versus}$$
$$H_A: T > P \qquad (1).$$

The single most important statistical issue in designing a clinical trial is to minimize bias. Typically this is achieved by using the blinding and randomization techniques. Such trials are often referred as well-controlled clinical trials.

In general, patients recruited into a clinical trial do not represent a random sample of the general patient population. Hence the generalization of the efficacy findings of the trial to general patient population should be considered with the medical feasibility, not purely through statistical justification. In addition, the effect size of the test treatment in the general population may not be covered by the estimation.

II. Historical-Controlled Clinical Trial

Often there are situations in which placebo control becomes unsuitable as the reference treatment in a clinical trial because of ethical reason or patient recruitment difficulty. Alternative controls will be used instead. With historical control, patients are recruited to receive the test treatment in either a single treatment trial or to be randomized to receive one of the multiple formulations of the test treatments. In either setting, test treatment is compared with assumed placebo effect or untreated groups of the historical database. The comparison may be carried out by direct comparison across trials for testing

$$H_0: T = P_H \text{ versus}$$
$$H_A: T > P_H \qquad (2),$$

where P_H is the expected placebo effect of the historical trials, or by using a one-sample test against the following null hypothesis

$$H_0: T = P_0 \text{ versus}$$

$$H_A: T > P_0 \qquad (3),$$

where P_0 is the assumed expected value of placebo effect derived from historical data.

For testing against the null hypothesis (2), the asymptotic test uses the following test statistic

$$z = (\hat{T} - \hat{P}_H)/\text{s.e.}\,(\hat{T} - \hat{P}_H).$$

H_0 is rejected if $z > z_{1-\alpha}$.

For testing against H_0 (3), the asymptotic test uses the following test statistic

$$z = (\hat{T} - P_0)/\text{s.e.}\,(\hat{T}).$$

Note that there are a few important differences among the hypotheses (1), (2) and (3). In testing hypothesis (1), the test treatment is compared with the concurrent placebo treatment P in the placebo control trial. In historical control trial, the test treatment is compared with the historical placebo. This difference plays an important role in the creditability of well-planned historical-controlled trials and the interpretation of the results. Let us examine the parameters to be tested in (1) and (2).

$$T - P = (T - P_H) + (P_H - P) \qquad (4).$$

The term on the left hand side of (4) represents the parameter in (1) and the first term on the right hand side represents the parameter to be tested in (2), P can also represent the common expected non-existed placebo in historical trials. Hence, there is a bias of $(P_H - P)$, when using the comparison of test treatment with historical control to interpret the comparison in (2). The bias is expected to be small if historical trials are many and the confidence intervals of P_H are consistent across the historical trials. Often in this case, the bias is considered to be negligible. This is often called constancy assumption of placebo mean. Under the constancy assumption, T – P can be estimated by $\hat{T} - \hat{P}_H$ with $\text{s.e.}(\hat{T}-\hat{P}_H)=\sqrt{[\text{Var}(\hat{T})+\text{Var}(\hat{P}_H)]}$.

The relationship of the parameters used in hypotheses (1) and (3) can be represented as follows,

$$T - P = (T - P_0) + (P_0 - P).$$

Hence the bias of using historical control trial to infer the difference between the test treatment and concurrent placebo is $(P_0 - P)$. Under the constancy assumption, the bias is 0.

The choice of P_0 is crucial in this setting. In general, the variance of the estimate of the right hand side is $\text{Var}(\hat{T}) + \text{Var}(\hat{P})$. When P_0 is the known true placebo mean and under the constancy assumption, bias $(P_0 - P) = 0$ and T – P is estimated by $\hat{T} - P_0$ with variance $\text{Var}(\hat{T})$. However, in practice, P_0 is estimated from the data of historical trials. If the historical control trials (k=1, …, K) share the same placebo mean, i.e., $P_0 = E(P_{Hk})$, $\text{Var}(\hat{P}_0) = [\Sigma_k n_k \text{Var}(\hat{P}_{Hk})]/(\Sigma_k n_k)$. However, if $P_0 = P$, but $E(P_{Hk}) \neq E(P_{Hk'})$ for some k and k', $\text{Var}(\hat{P}_0)$ can be estimated from a random effect model. In either case, a properly selected upper confidence limit $\hat{P}_0^U$ of P_0 is used. In the case when the number of historical trials is small and random effect model is not applicable, often the highest upper confidence limit of P_0 among all historical trials is used.

III. Active-Controlled Clinical Trial

An active-controlled clinical trial is often used when a placebo-controlled is not suitable while a standard treatment is available. The efficacy of the test treatment may be established by rejecting

$$H_0: T = A \text{ by showing } H_A: T > A,$$

which is essentially rejecting the null hypothesis in (1) with R=A, a standard active treatment. However, in many situations, the data do not support the superiority claim and the efficacy of the test treatment needs to be established through comparison with a non-concurrent placebo "P",

$$H_0: T = \text{"P"} \text{ versus}$$
$$H_A: T > \text{"P"} \qquad (5).$$

This approach is often called non-inferiority testing. In order to infer the relationship between T and "P", the active control A is served as a linkage in such a way

$$T - \text{"P"} = (T - A) + (A - A_H) + (A_H - P_H) + (P_H - \text{"P"}) \qquad (6),$$

where A is the concurrent active control, P is the non-concurrent placebo, A_H is the historical active control and P_H is the historical placebo respectively.

Under the constancy assumption of the effect of active control, $A - \text{"P"} = A_H - P_H$, (6) can be rewritten as

$$T - \text{"P"} = (T - A) + (A_H - P_H) \qquad (7).$$

Hence the hypotheses to be tested for efficacy are replaced by

$$H_0: T - A = -(A_H - P_H) \text{ versus}$$
$$H_A: T - A > -(A_H - P_H).$$

A typical approach for inferring hypotheses (5) is to test the following hypotheses

$$H_0: T - A = -\delta \text{ versus}$$
$$H_A: T - A > -\delta \qquad (8),$$

where δ is often called the non-inferiority margin and is determined to represent the value determined by $(A_H - P_H)$.

Note that:

Formulation in (7) is similar to (2) in that the parameters on the left hand side of the hypotheses are of the current trial and the parameters on the right hand side of the hypotheses are of the historical control trials. The statistical considerations involved in testing the null hypothesis in (2) are also applicable here.

- Formulation in (8) is similar to (3) of historical control trials. Hence, the statistical considerations involving testing (3) are also applicable here.
- Bias, due to imbalance of baseline factors in historical control trials because of lack of randomization, may be minimized if not eliminated because of the randomization within the trials. However, the possible bias in comparison of the parameters of different clinical trials may still exist.
- In contrast to the constancy assumption on mean response of the treatment (i.e. placebo) in historical control trials, the constancy assumption is on the effect size of the active control.

Hence, when the number of historical control trials with placebo arm is large but the number of historical trials with the standard active treatment is small or the effect size of active treatment varies greatly among the historical trials, the advantage of active control design over historical control design may need to be reconsidered.

Summary

We showed that strong assumptions are required beyond the simple blinding and randomization techniques to linking the current trial to historical data in order to be able to assess the efficacy of a test treatment in historical control trials or in non-inferiority active control trials. These assumptions are difficult to verify and hence become major weakness in interpreting the study results. The similarity with respect to the statistical issues between historical control design and non-inferiority active control design makes it

almost impossible to consider non-inferiority active control design differently from historical control design in both design and analysis.

* The views expressed in the article are those of the authors and not necessarily of FDA. The work is partially supported by an FDA funded Review Science Research Grant (#RSR-01-20).

Active-control Trials: A Linguistic Problem

By Janet Wittes, Ph.D.
Statistics Collaborative, Inc.

Active-control Trials: Is the Problem Statistical?

When clinicians toss us the ball saying, "This is a statistical problem" and we statisticians lob it back with, "No, this is a clinical problem," we are all in trouble. So it is with active controlled trials. The conundrum we face in designing and analyzing such trials stems, I believe, from tangled language and purpose. In these brief remarks, I will describe the linguistic problems we, both statisticians and clinicians, face in designing, analyzing, and interpreting an active controlled trial. Such trials come in two flavors, those that attempt to show superiority of the new intervention and those that aim to show "equivalence" or "non-inferiority". The former poses little problem; the latter often leads us into an inferential morass.

To start with the easy case, suppose one is trying to demonstrate the superiority of a test drug over a standard treatment. The task is inferentially clear if previous randomized clinical trials have shown the standard treatment superior to placebo or even in the absence of data on its efficacy, if the standard is so widely used that control against placebo would raise ethical eyebrows. For example, the CONVINCE trial, which is comparing controlled-onset extended-release (COER) verapamil to standard of care in persons with hypertension, is testing the hypothesis that COER-verapamil leads to a reduction in mortality relative to standard of care [1]. The trial is testing the simple null hypothesis that the incidence of fatal or nonfatal myocardial infarction, fatal or nonfatal stroke, or cardiovascular disease-related death in the two arms is equal against the natural two-sided alternative. If the data lead to rejection of the null hypothesis, then COER-verapamil will have been shown to lower the rate of clinical endpoints relative to the active control arm where, in this case, is standard of care. The fact that the trial has used an active control will have rendered the conclusion more relevant to practice than had the trial used a placebo.

The situation becomes much more difficult for trials that aim to show "equivalence" or "non-inferiority" of the test agent to the active comparator. In discussing such trials, we must come to grip with the deceptive language inherent in the terms "equivalence" and "non-inferiority". A normal person might well assume that "equivalent" means "the same as" and non-inferior" means "no worse than"; in clinical trial-speak, however, "equivalent" means "not unacceptably different from" and "non-inferior" means "not unacceptably worse than". Our failure to adopt honest language obfuscates the hypotheses we are testing and casts an unrealistically favorable light upon our results. Them's fighting words, the reader might say. And I will respond, "yes", but deceptive language lies at the root of misinterpretation.

The "not unacceptably worse than" trial is typically relevant to clinical endpoints while the "not unacceptably different" trial applies to surrogate markers. Consider a trial of a new vaccine for influenza compared to one already marketed. If the endpoint is incidence of disease, then the appropriate design is the "not unacceptably worse than" trial. Suppose the marketed product has an efficacy of 70 percent where vaccine efficacy is defined as 1-incidence in vaccine/incidence in placebo. If recipients are expected to find the new vaccine more tolerable, public health workers may believe that an efficacy of only 60 percent is "not unacceptably worse than" than the marketed vaccine and therefore may urge approval of such a vaccine. Of course, if the new vaccine shows higher efficacy than the marketed one, so much the better. The "not too much worse than" trial allows rejection of the null hypothesis if the new vaccine is in fact superior to the previous one.

On the other hand, if the endpoint is not clinical efficacy but some marker of immune response, then one might demand that the new vaccine have properties similar to that of the marketed agent. One would specify a range that represents "not unacceptably different from". For example, the marketed agent may confer a mean eight-fold increase in an immune marker; the "not unacceptably different" interval may be four-fold to sixteen-fold. Observing a 32-fold increase in the marker would then be a failure to show "not unacceptably different from" even if, at first blush, a 32-fold increase seems intuitively better than an eight-fold increase. The problem with presuming larger means better in the absence of data is that one cannot be certain how changes in surrogate markers affect changes in clinical endpoints.

Many people have dealt with the challenges in designing a "not unacceptably different from trial" (a.k.a., an equivalence trial) abound. One must select the margin of indifference narrow enough to exclude a clinically relevant degradation of effect but wide enough too allow a feasible sample size [2-4]. As Temple and Ellenberg have described, one must think about "assay variability", the possibility that the comparator agent is less effective in the trial being designed than in the trials that demonstrated its efficacy [5]. One must avoid finding no difference from standard by virtue of running a sloppy trial; in a superiority trial, sloppiness pulls the data towards the null hypothesis while in a "not unacceptably worse" trial, sloppiness makes two otherwise different drugs appear more similar than they in fact are.

Finally, both clinicians and statisticians should question the purpose of the trial. If the margin of "equivalence" is too wide and the active control too variable in its efficacy, the data may formally lead to rejection of the null hypothesis of "equivalence" but fail to show convincingly that the test agent is an acceptable substitute for the agent already in use. We as statisticians must not allow our well-honed statistical machinery to appear to "prove" a hypothesis that is not clinically important. And let us resist the words "equivalence" and "non-inferiority", for they mean not what they say.

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Some Upcoming Statistical Meetings

DIA Innovative Statistical Strategies in the Pharmaceutical Industry,
Mar. 11-13, 2001, Savannah, GA.

ENAR Spring Meeting "The Impact of Technology on Biometrics",
Mar. 25-28, 2001, Charlotte, NC.

3rd Cross-Straight Statistics and Probability Conference and CIPS 2001 conference,
April 14-15, 2001, Academia Sinica, Taipei,
Website: http://www.stat.sinica.edu.tw/cips2001/bulletin-1.htm

23th Annual Midwest Biopharmaceutical Statistics Workshop, Ball State University,
May 21-23, 2001, Muncie, Indiana.
Co-sponsored by the Biopharmaceutical Section of the American Statistical Association.

Society for Clinical Trials,
May 19-23, 2001, Denver, CO.

The meeting will include topics of interest to researchers in academia, private industry and government that focus on trial design, analysis, organization and management; and quality control and cost issues in clinical trials. The program consists of plenary, contributed paper, poster and pre-conference workshop sessions. Deadline for abstract submission is December 1, 2000. For more information about the Society for Clinical Trials (SCT) or about joining the SCT and receiving the peer-reviewed journal Controlled Clinical Trials, visit the SCT web site at www.sctweb.org.

ICSA 2001 Applied Statistics Symposium, Details see Meeting Announcement, page 42.
June 7-9, 2001, Chicago, IL.

Interface 2001, The 33rd Symposium on the Interface of Computer Science and Statistics,
June 13-16, 2001, Orange County, California.

DIA Annual Meeting,
July 8-12, 2001, Denver, CO.

Joint Statistical Meetings,
August 5-9, 2001, Atlanta, GA.

The 5th ICSA International Conference,
August 17-19, 2001, University of Hong Kong, Hong Kong.

ICSA 2002 Applied Statistics Symposium, details in the next issue of ICSA Bulletin.
June 6 - 8, 2002, Philadelphia, PA.

❖ ANNOUNCEMENT ❖

ICSA 2001 APPLIED STATISTICS SYMPOSIUM
June 7-9, 2001
Congress Hotel, Chicago, Illinois

For the first time in the history of ICSA, the 11th annual ICSA symposium will be held at Chicago. Chicago is the center of finance and industries in the mid-west area. It is the home of several fine academic institutions. The city is also known for its architectural beauty. All interested are invited.

Symposium Theme: **New Frontier of Statistics: Statistics in Genomics, Statistical Finance and Data Mining.**

Featured Plenary Speakers:
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- Wen-Hsiung Li, George Beadle Professor, Ecology and Evolution, University of Chicago
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- Wing Hung Wong, Professor of Statistics and Professor of Computational Biology, Harvard University

Short Courses (tentative):
- Clinical Trial Simulation
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- Survival Analysis

For information, online registration and abstract submission, please visit to http://www.icsa.org.

DATE: June 7 to 9, 2001, short courses on June 7, Thursday and sessions on Friday and Saturday

LOCATION: Congress Hotel, at Grant Park in Chicago. The hotel is a landmark in downtown Chicago.

ACCOMODATION: $115 single and $125 double at Congress Hotel. $32 single and $44 double at UIC dormitories.

BANQUET/Karaoke: Will be held at a restaurant in the Chinatown in Chicago.
Chicago Architecture Boat Tour: free to all participants and guests.

STUDENT AWARD: Students may submit research articles to the Program Committee. A cash award will be offered as assistance to the student's travel funding to attend ICSA symposium. Up to four awards at $400 each will be available. See announcement in this bulletin for details.

Please Note: The symposium dates have been changed to June 7-9, 2001, from June 8-10, 2001 announced previously

CALL FOR PAPERS

ICSA 2001 Applied Statistics Symposium
June 7-9, 2001

The Program Committee of the ICSA 2001 Applied Statistics Symposium invites you to submit statistical papers for presentation at the Symposium. Abstracts for invited and contributed papers are due **March 30, 2001**.

Please submit abstract through our website at
http://ebusiness.cba.uic.edu/icsa2001 or send abstract to

Professor Rong Chen
Dept. Information and Decision Sciences (MC 294)
University of Illinois at Chicago
Chicago, IL 60607

The abstract should include the name, work affiliation, mailing address, telephone number, fax number, and e-mail address of the author, and should not exceed 200 words and should have minimum mathematical formulas.

ICSA 2001 Applied Statistics Symposium
Student Awards and Travel Fellowships

The Program Committee of the 2001 ICSA Applied Statistics Symposium sponsors student awards and travel fellowships. The purpose of the award is to encourage ICSA student members to participate and present their research work at the annual meeting.

All ICSA members who are degree candidates in 2001 at accredited institutions and are able to present the manuscript at the 2001 Symposium are eligible to apply.

Award: Up to three (3) awards of $400 each are available.

Submission of application: The applicant will mail the following items:

1. Cover letter
2. 5 copies of the manuscript with no identification of the author
3. Title page with author's name, institution, mailing address, phone number, and e-mail address
4. Two copies of completed ICSA Applied Statistics abstract form
5. Two copies of ICSA membership application form, if the student is not a member.

to any one of the three members of the Program Committee:

Jianqing Fan, e-mail address: jfan@math.ucla.edu
Jun Liu, e-mail address: jliu@stat.stanford.edu
Ruey Tsay, e-mail address: rst@gsbrst.uchicago.edu

Please contact the Program Committee member for his mailing address.

The subject of the research must be relevant to statistics. The student author must be the primary author of the research presented in the manuscript.

The manuscript should be double-spaced using Biometrics or JASA guidelines for authors. The text of manuscript, excluding tables and figures, should not exceed 20 pages. Use one inch margins and no small than 12-point type.

Deadline: The manuscript must be postmarked no later than January 31, 2001.

Award announcement: The winners of the awards will be notified by March 15, 2001.

INTERNATIONAL CHINESE STATISTICAL ASSOCIATION

The 5th ICSA International Conference, Hong Kong, August 17-19, 2001

Date : August 17 – 19, 2001 (Prior to the 53rd Session of ISI in Seoul)

Place : The University of Hong Kong, Hong Kong

Keynote Speakers : Professors Peter Hall and Tze-Leung Lai

Registration Fee (Including Reception, Banquet, Coffee and two Lunches)

	On or before April 1, 2001	*After April 1, 2001*
Regular	U.S. $150	U.S. $200
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Papers, both theoretical and applied, are invited for presentation at the conference. Please send a copy of the abstract of no more than 200 words (without any symbols or formulas) to the following address (preferably by e-mail or on disk) before April 1, 2001 along with your registration form and fee. A sample abstract can be found in the website of the conference:

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The 5th ICSA International Conference, Hong Kong, August 17-19, 2001

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The ICSA Nominating and Election committee invites you to nominate candidates for the 2000 President-elect and five members of board directors. Your input is important as the success of ICSA depends on strong leadership which can be best produced from a broad pool of candidates of these two offices. We are looking forward to receiving nominees from you. Please check with nominees about their qualifications before you submit their names to Mei-Cheng Wang, the Committee Chair. Nomination deadline is February 28, 2001. In your nomination, please include for each nominee: name, affiliation, address, and a paragraph of reasons for your nomination. You may nominate at most one candidate for the President-elect and unlimited number of candidates for the board directors.

To make the evaluation process efficient, nomination through emails is encouraged. Please submit your nomination to

<Mei-Cheng Wang> mcwang@jhsph.edu

The minimum qualifications for the President-elect and board directors are as follows:
The candidate for President-Elect must
1. have been an active member for at least three years
2. have held office of ICSA (e.g. director or committee member)
3. commit to chair board meetings during the year of presidency
4. commit to attend at least one board meeting per year as president-elect and past president (exception can be made for candidates outside North America).

The candidate for board director must
1. be a current ICSA member
2. if resides in North America, commit to attend at least one board meeting per year; if resides in Taiwan or HK, attend at least two board meetings in three years; if resides in China, attend at least one board meeting in three years.
3. when unable to attend the board meeting, send a proxy.

Nominating and Election Committee:
Chao Agnes Hsiung, Dennis K-J Lin, Jen-Pei Liu, Frank Shen, Mei-Cheng Wang (Chair)

Mei-Cheng Wang
Dept. of Biostatistics
School of Public Health
Johns Hopkins University
615 N. Wolfe St.
Baltimore, MD 21205
Tel: 410-955-7775
Fax: 410-955-0958
Email: mcwang@jhsph.edu

Nominations for 2001 ICSA Awards

The ICSA Awards Committee invites you to nominate candidates for the 2001 ICSA Awards. The committee is looking for "a few good members" who have made significant contributions to the Association. Examples of candidates are members who have:

1. Successfully organized and conducted a professional meeting

2. Effectively led the ICSA activities

3. Held a strong and effective editorship (including associate editorship) for Statistica Sinica

4. Substantially increased the ICSA memberships

5. Initiated and implemented a policy which resulted in a substantial visibility for the ICSA

6. Established strong ties with other professional societies and co-sponsored statistics activities with them.

In your nomination please include the nominee's name, title, address, a description of his/her significant contributions and the names of other ICSA members or statisticians who are familiar with the nominee's contributions. Once the awards are decided, they will be presented in August 2001 in Atlanta/Hong Kong.

The committee will select the most deserving candidates, who have made multiple significant contributions resulting in a strong positive impact to the Association, to receive awards. Preference will be given to those who have not previously received such an award.

Your nominations must be received no later than February 28, 2001. Please send your Nominations to:

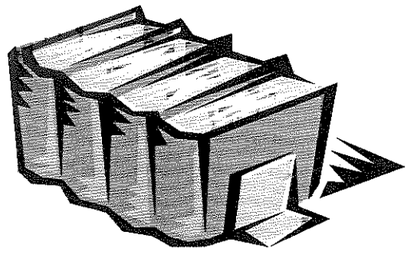
Cun-Hui Zhang
Department of Statistics
Rutgers University
Hill Center, Busch Campus
Piscataway, NJ 08854-8019

ICSA BOOK & JOURNAL DONATION COMMITTEE

Requests your participation in donating your statistical books and journals, to the university libraries in the developing countries.

Books must be in good condition; journals must be in complete volumes. ICSA will reimburse the mailing cost; you supply books, boxes, and time. Donation of books and journals will be issued a donation receipt from ICSA. It is preferred to have at least 10 books or several years of journal in one shipment.

During last year, we sent 54 books and 9 years of Statistica Sinica to 5 different institutions in China.
the mailing cost.



If you are interested in helping the libraries in need, please contact Professor Tar Timothy Chen at either tchen001@umaryland.edu or t-chen-10@alumni.uchicago.edu. Regular mailing address –Dr. T. Timothy Chen, Professor and Head of Biostatistics Section, University of Maryland Greenebaum Cancer Center, 22 South Greene Street, Room N9E28, Baltimore, Maryland 21201. You need to send a list of books with information about authors, book title, year of publication, and the name of publisher.

If your library would like to receive donated books and journals, please contact Professor Chen to indicate your interest. This service is on the first come, first serve basis. So advance contact is necessary.

REGIONAL ACTIVITY

Some Events of the Hong Kong Statistical Community in 2000

Hailiang Yang

Here I report some information about the activities and events of the Hong Kong statistical community in 2000. I will list them chronologically.

Centre of Financial Time Series of the University of Hong Kong Workshop on Value-at-Risk, February 26, 2000.
The workshop was organized by the Centre of Financial Time Series of the University of Hong Kong. Professor Paul Embrechts of ETH Zurich of Switzerland was invited to conduct the workshop. The participants included faculty members and graduate students from Hong Kong University and other sister institutions in the tertiary, as well as some specialists from industries and the government.

The 4th International Conference on Monte Carlo and Quasi-Monte Carlo Methods in Scientific Computing, Hong Kong Baptist University, November 27- December 1, 2000.
11 plenary speakers from all over the world participated. They were: S. Asmussen, M. Avellaneda, K.T. Fang, P.W. Glynn, C. Lecot, X.L. Meng, H. Niederreiter, E. Novak, I. H. Sloan, S. Tezuka and J. S. Wang. The conference program contained 8 special sessions of four talks each on topics of current interest and over 60 contributed presentations. The proceedings of the conference will be published by Springer-Verlag.

The fifth ICSA International Conference will be held at the University of Hong Kong from August 17 to 19, 2001.
The Programme/Organising Committee includes Professors W.K. Li (Programme Chair), H. Tong, K.T. Fang, L.K. Chan, X.L. Meng, J.Q. Fan, M.G. Gu, K.W. Ng, W.S. Chan, L.Zhu and Mr. F. Ho. The keynote speakers are Professors P. Hall and T. L. Lai. Further information can be found from Website:
http://www.hku.hk/statistics/ICSA2001/

Statistical Workshops and Conferences in Taiwan, 2000

C. Andy Tsao

Chinese Statistical Society (CSS), Chinese Institute of Probability and Statistics (CIPS), Directorate-General of Budget, Accounting and Statistics (DGBAS) organize statistical conferences jointly with universities every year. Besides these conferences, there are conferences and workshops on special topics.

CIPS Annual Conference. 2000/4/15. Feng-Chia University, Taichung. Organizers: CIPS, Fung-Chia University (Department of Statistics and Institute of Statistics and Actuarial Science).

CSS Annual Meeting and 9th Southern Statistical Conferences. 2000/5/27-5/28. Cheng-Kung University, Tainan. Organizers: CSS, Cheng-Kung University (Department and Institute of Statistics). Topics: Bayesian Statistics, statistics in actuarial science, financial statistics, etc.

3rd Conference on Methodology and Application in Survey. 2000/10/19-10/20. Academia Sinica, Taipei. Organizer: Office of Survey Research, Academia Sinica. Topics: Web-survey, email survey, opinion polls and survey methodology.

Recent Advancement in Biopharmaceutical Statistics: Clinical Trials and Drug Development. 2000/12/16-12/16. National Health Research Institute (NHRI), Taipei. Organizer: Division of Biostatistics at NHRI. Topics: Sample-size re-estimation, statistics in pharmacogenetics, etc.

Interested readers are directed to the following Websites:

http://www.nhri.org.tw/biostat/drug/
http://www.stat.ncku.edu.tw/Liang.html#reach
http://www.stat.ncku.edu.tw/conference/index
http://www.stat.fi/isi99
http://www.nso.go.kr/isi2001

The list is by no means exhaustive but simply serves as an outline.

STATISTICS' DELIGHT

統計趣聞

統計謎語

- 如果統計是從有限的資料、線索尋找答案的一門學問，則謎語也可以看做是統計問題。

根據以下的提示，射一統計相關語

1。 梳頭

2。 混血種

3。 道家思想（猜一統計學家）

4。 萬綠從中一點紅

5。 一顆老鼠壞了一鍋粥

6。 頂司管下司，鋤頭管畚箕

7。秦時明月漢時關，萬里長征人未還，但使龍城飛將在，不教胡馬渡陰山

答案

1.Smoothing
2.Mixed-Effect
3.Yi-Tsong (莊昜)
4.Outlier
5.Outlier Contamination
6.Order Restricted Inference
7.Long-Term Trial with Stopping Boundary

Brain Teaser

☺☺☺

Q: You have a rectangular cake out of which has been cut a rectangular slice (The missing rectangle is not necessarily along the center line). You have a knife with which you can make one cut in the cake. How do you cut it so that you bisect both the rectangle of the cake and the rectangle of the missing slice?

☺☺☺

♥♥♥ HOW MANY STUDENTS DOES IT TAKE TO CHANGE A LIGHTBULB AT ♥♥♥

♥Vanderbilt: Two, one to call the electrician and one to call daddy to pay the bill.

♥Princeton: Two, one to mix the martinis and one to call the electrician.

♥Brown: Eleven, one to change the lightbulb and ten to share the experience.

♥Dartmouth: None, Hanover doesn't have electricity.

♥Cornell: Two, One to change the lightbulb and one to crack under the pressure.

♥Penn: Only one, but he gets six credits for it.

♥Columbia: Seventy-six, one to change the lightbulb, fifty to protest the lightbulb's right to not change, and twenty-five to hold a counter protest.

♥Yale: None, New Haven looks better in the dark.

♥Harvard: One, he holds the bulb and the world revolves around him.

♥MIT: Five, one to design a nuclear powered one that never needs changing, one to figure out how to power the rest of Boston using that nuked lightbulb, two to install it, and one to write the computer program that controls the wall switch.

♥Stanford: One, dude.

♥Georgetown: Four, one to change it, one to call Congress about their progress, and two to throw the old bulb at the American U. Students.

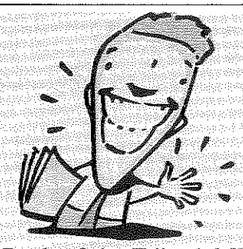
♥Duke: A whole frat, but only one of them is sober enough to get the bulb out of the socket.

♥Williams: The whole student body--when you're snowed in, there's nothing else to do.

Brain Teaser - Answer

☺☺☺

The mathematical answer is that any line through the midpoint of a rectangle bisects the rectangle. Cut along a line connecting the midpoints of the cake and the missing rectangle. This will bisect both of them. The "outside the box" answer is to forget all about rectangles, turn the cake on its side and slice it in half, bisecting both the cake and the rectangle of the missing slice.



From the Desk of the Editorial Working Committee

Congratulations to the Following ICSA Members Who Were Elected as ASA, IMS, and COPSS Fellows or Receiving Awards in 2000

ASA Fellows:

Danyu Lin, Professor of Biostatistics, University of Washington:
For fundamental contributions to statistical theory and methods, especially in survival analysis and clinical trials, and for extensive editorial service.

Xihong Lin, Associate Professor of Biostatistics, University of Michigan:
For contributions to the development of semi-parametric and hierarchical models; for innovative applications of statistics to biomedical problems; and for service to the profession.

Suojin Wang, Professor of Statistics, Texas A & M University:
For research in the theory and practice of small-sample inference via higher order methods, sample surveys, and missing and mis-measured data; and for excellence in teaching.

Heping Zhang, Associate Professor of Biostatistics, Statistics, and Child study, Yale University:
For significant contributions to methodology in non-parametric classification and non-linear regression; for influential work in statistical genetics; and for applications in epidemiology and psychiatry.

Section and Chapter Awards:

Section of Bayesian Statistical Science

Mitchell Prize

Jun Liu, Professor of Statistics, Stanford University, Stanford, California.

COPSS Awards:

Presidents' Awards

Jianqing Fan, Professor, Department of Statistics, University of California, Los Angeles.

http://merlot.stat.uconn.edu/~ims/bulletin/IMSBulletineoct2000/node27.html
http://merlot.stat.uconn.edu/~ims/bulletin/IMSBulletineoct2000/index.html

WELCOME NEW MEMBERS

We would like to welcome new members who joined between July and December 2000.

An, Bob	Au, Tan	Ge, Nanxiang	Hsu, Pei-Whe
Hu, Peter	Li, Na	Li, David	Lin, Yong
Liu, Shaocheng	Lo, Yungtai	Luo, Xiaolong	Poetzelberger, Klaus
Shao, Quanxi	Shiue, Sarah	Tan, Kenseng	Wang, Daniel Z
Wang, Yamei	Wu, Yu	Xie, Minyu	You, Min
Zhang, Donghui	Zhang, Jerry	Zitikis, Ricardas	

DONATIONS Between July 2000 and December 2000, we have received donations from:
Yeh, Chiao

MEMBERS' ACTIVITIES

News from ICSA Members in Hong Kong

Professor W.K. Li was elected as the president of the Hong Kong Statistical Society. Dr. Li is a professor of the Department of Statistics, The University of Hong Kong. Mr. K.C. Leung of Census and Statistics Department was elected as Vice-president.

The Hong Kong Statistics Society has registered as a corporation. The new society will handle the public examinations of certified professional statisians in collaboration with the Royal Statistical Society of the UK.

Professor Y. Lam has retired. Professor Lam was a professor and department head in the Chinese University.

Professor J.Q. Fan from the University of California has joined the Department of Statistics in the Chinese University of Hong Kong as the Chair of statistics and department head.

Professor H.S. Lau from the Oklahoma State University has joined the Department of Management Sciences in the City University of Hong Kong as Chair professor of Management Sciences.

Professor N.F. Chan from the Carnegie Mellon University has joined the department of Statistics as chair professor and director of the risk management science program.

News from ICSA Members in Canada

EUR Professor Jim J. S. Huang has retired from the Department of Mathematics, the University of Guelph, Guelph, Ontario, Canada and has accepted a one year position as Visiting Professor at Department of Statistics, University of California at Riverside. His old email address is still in effect, but here is the new one: jhuang@ucrstat3.ucr.edu
(O) 909-787-3286
(H) 909-328-8608

FACULTY POSITION

Department of Statistics
University of California at Davis

The Department of Statistics invites applications for a position, starting July 1, 2001 or a later date to be arranged. The position is at tenure track Assistant Professor level, or at Associate Professor level with tenure, depending on qualifications. Applicants must have a Ph.D. in Statistics, Biostatistics, Mathematics or a related field and an outstanding research and excellent teaching record for appointment with tenure, or demonstrated interest and ability to achieve such a record for a tenure track appointment. Preferred research areas are analysis of large and complex data sets, biostatistics, or computational statistics. Candidates with demonstrated research interest in bioinformatics are strongly encouraged to apply. The successful candidate will be expected to teach at both the undergraduate and graduate levels. UC Davis has launched a Bioinformatics initiative and plans to establish a graduate program in Biostatistics, in addition to the existing Ph.D./MS program in Statistics. Information about the department and programs offered can be obtained from the website http://www-stat.ucdavis.edu/. Send letter of application, including a statement of research interests, curriculum vitae with publication list, at least three letters of reference, relevant reprints/preprints, and transcripts (applicants with Ph.D. obtained in 1999 or later) to:

Chair, Search Committee
Department of Statistics
1 Shields Avenue
University of California
Davis, CA 95616.

Review of applications will begin on January 1, 2001, and will continue until the position is filled. The University of California is an affirmative action/equal opportunity employer with a strong institutional commitment to the achievement of diversity among its faculty and staff.

Investigator and Postdoctoral Fellow Positions in Biostatistics and Bioinformatics

National Health Research Institutes (NHRI)
Taiwan, R.O.C.

The National Health Research Institutes (NHRI) is a rapidly growing non-profit organization supported by the Government of R.O.C.. **The Division of Biostatistics and Bioinformatics** in the NHRI is seeking outstanding researchers for the positions at the levels of Assistant Investigator, Associate Investigator, and Investigator(the equivalent of Assistant Professor, Associate Professor, and Professor in Universities). These are fully funded positions with sufficient opportunities for independent research. Posdoctoral Fellow positions are also available.. Candidates should have a Ph.D. or equivalent degree in **statistical science**, **computational biology**, **computer science** or related fields. Good skills in problem-solving, interpersonal communication and coordination will be a plus.

The Division actively engages in NHRI intramural and extramural research design, data management and analysis, and commits to the advancement of biostatistics and bioinformatics research. Current research includes clinical trials, genetic studies and environmental epidemiology studies etc.. Bioinformatics Core Laboratory is established by the Division to facilitate genomic studies.

We are establishing a multi-disciplinary group to work together analyzing many interesting data in a variety of studies to elucidate health related scientific problems. **Application should include:** A letter of intent, curriculum vitae with publication list, a brief research proposal, reprints of selected publications, and three reference letters sent directly to

Dr. Chao A. Hsiung, Director
Division of Biostatistics and Bioinformatics
National Health Research Institutes
128 Yen-Chiu-Yuan Road, Sec II, Taipei 115, Taiwan, R.O.C.
Tel: 886-2-2653-4401 ext. 7110 Fax: 886-2-2789-0253
E-mail: hsiung1@nhri.org.tw
NHRI web site - http://www.nhri.org.tw

International Chinese Statistical Association

01/08/01 Profit and Loss
January through December 2000

		Jan - Dec '00
Ordinary Income/Expense		
Income		
Advertisement	1,570.00	
Contributions Income		
Unrestricted	590.00	
Total Contributions Income		590.00
Membership Dues	17,170.00	
Short Course 2000	820.93	
Total Short Course		820.93
Total Income		20,150.93
Expense		
Board Meeting	217.62	
Casual Labor	888.00	
Contributions		
ASA	500.00	
Statistica Sinica	4,372.85	
Total Contributions		4,872.85
ICSA at ASA meeting		
Banquet	500.00	
Total ICSA at ASA meeting		500.00
Internet Registration	35.00	
Licenses and Permits	95.00	
Office Supplies	15.86	
Postage and Delivery		
Announcement	590.05	
Ballot	515.91	
Directory	4,225.98	
Postage and Delivery - Other	319.80	
Total Postage and Delivery		5,651.74
Printing and Reproduction		
Directory	3,688.00	
Jan. Bulletin	2,588.75	
Jul. Bulletin	6,569.73	
Total Printing and Reproduction		12,846.48
Professional Fees		
Accounting	450.00	
Database design	4,000.00	
Total Professional Fees		4,450.00

Reimbursed Expenses		
Banquet Fee Collected	-500.00	
Total Reimbursed Expenses		-500.00
Supplies		
Office	233.42	
Supplies - Other	458.94	
Total Supplies		692.36
Travel & Ent		
Meals	35.00	
Mileage	315.25	
Tolls	48.35	
Total Travel & Ent		398.60
Web Page Hosting	1,279.55	
Total Expense		31,443.06
Net Ordinary Income		11,292.13
Other Income/Expense		
Other Income		
Interest Income	3,831.66	
Total Other Income		3,831.66
Net Other Income		3,831.66
Net Income		7,460.47

International Chinese Statistical Association

01/08/01 Balance Sheet
As of December 31, 2000

		Dec 31, '00
ASSETS		
Current Assets		
Checking/Savings		
Checking	1,208.37	
Saving	80,725.79	
Total Checking/Savings		81,934.16
Total Current Assets		81,934.16
TOTAL ASSETS		81,934.16
LIABILITIES & EQUITY		
Equity		
Retained Earnings	89,394.63	
Net Income	-7,460.47	
Total Equity		81,934.16
TOTAL LIABILITIES & EQUITY		81,934.16

ICSA SYMPOSIUM ACCOUNT (JAN2000 – DEC2000)

Report date: January 05, 2001
From: H.M. James Hung (Treasurer, ICSA Applied Statistics Symposium Account)

Item	Credit	Debt	Balance
Symposium Account Balance (12/31/99)			**11,541.91**
2001 Symposium Starting Fund (3/24/00)		5,000.00	
Refund for overpaid dorm fee in 1999 ICSA Symp. (4/03/00)		10.00	
Service charge and check order		206.60	
Interest earned (1/00 - 12/00)	**47.54**		**6,372.85**
2000 Applied Statistics Symposium			
Income (total = $65,700.00)			
Starting fund	3,000.00		
Donation	24,400.00		
Registration	37,800.00		
Advertisement	500.00		
Expenses (total = $52,685.43)			
Registration refund		1,465.00	
Registration for ICSA		4,600.00	
Student award		600.00	
Short course instructor fee		4,500.00	
Banquet		11,834.68	
Embassy Suites		19,128.81	
Certificates, plaques, and banners and related		1,208.22	
Keynote speaker expenses		906.29	
ICSA board meeting expenses		986.35	
Half of remaining short course income to ICSA		820.93	
Other expenses (stationary, misc, committee, etc)		6,635.15	
Symposium Account Balance (12/31/00)			19,387.42

INTERNATIONAL CHINESE STATISTICAL ASSOCIATION

Membership Application / Renewal Form (2000)
Date _____

NAME (Last) (First)

English:

Chinese:

ADDRESS

Office:	Home:
City: State:	City: State:
Zip:	Zip:
Country:	Country:
Tel (O):	Tel (H):
Fax (O):	Fax (H):

E-Mail Address:

Highest Degree: Year Graduated:

University: Occupation/Title:

MEMBERSHIP FEES

Regular	US$40	_____
Student	US$20	_____
Permanent	US$400	_____
Spouse (50%)		_____ (Spouse Name _____)
Biometrics (Free)		_____
Donations		_____
Total Amount		_____

STATISTICAL AREA OF INTEREST (circle as many as you like):

A. Agriculture
B. Business/Econometrics
C. Computing/Graphics
D. Education
E. Engineering
F. Health Sciences
G. Probability
H. Social Sciences
I. Theory And Methods
N. Biostatistics

Please make checks payable to I.C.S.A.
Mail this form and a check to: I.C.S.A.
c/o Yi Tsong, Ph.D.
13215 lazy Glen Lane
Herndon, VA 22071
U.S.A.
(tsong@fda.cder.gov)

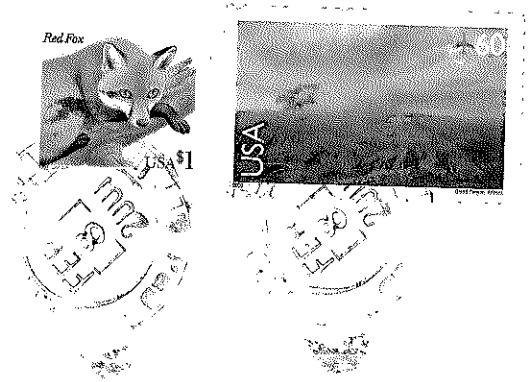
INTERNATIONAL CHINESE STATISTICAL ASSOCIATION

Information Sheet (2000)
Date _____

RECENT NEWS: (publications, research or teaching activities, job transfer, awards or honors received, etc.)

SUGGESTIONS :

I. C. S. A.
13215 Lazy Glen Lane
Herndon, VA 22071
U.S.A.



JIA-YEONG TSAY (P)
Organon Inc., 375 Mt. Pleasant Avenue
WEST ORANGE NJ 07052
United States