



Meta-Analysis in Drug Development



Speaker, Stephen Senn and organiser, Caro Badcock

On March 30–31 the NSW Branch proudly hosted the Meta-Analysis in Drug Development workshop presented by Prof Stephen Senn. Stephen was in Australia to attend ISI and was interested in presenting one of his courses while in the country.

The NSW Branch was the main organiser of the workshop. ARCS Australia (Australian Regulatory and Clinical Scientists) provided sponsorship

by advertising the workshop through their membership, in particular to the health economists. Covance Pty Ltd, a contract research organisation to the pharmaceutical industry, provided sponsorship in the form of preparation of course manuals.

The workshop was held at the Macquarie Graduate School of Management Conference Centre which proved an excellent venue.

Registrations were closed at 42 because of the desire to maintain a workshop environment. Attendees came from a range of organisations including large and small pharmaceutical companies such as Roche, GlaxoSmithKline, Pfizer and Eli Lilly; universities such as Monash, University of Queensland, University of Adelaide and Macquarie University, the NHMRC from University of Sydney; other government agencies such as CSIRO and the Department of Health and Ageing; contract research organisations such as Covance, Datapharm, Quintiles and MTag and consulting businesses such as Health Technology Analysts Pty Ltd and John Wlodarczyk Consulting Services indicating that the workshop was marketed to the right audience.

Stephen was originally from Switzerland and has been the Professor of Statistics at the University of Glasgow since 2003. He was Professor of Pharmaceutical and Health Statistics at University College London from 1995–2003. He has also worked in the Swiss pharmaceutical industry, for the National Health Service in England and previously as a lecturer in Scotland. Stephen was the first recipient of the George C Challis award for Biostatistics of the University of Florida. He has written three books: *Cross-over Trials in Clinical Research* (1993) (second edition 2002), *Statistical Issues in Drug*

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Meta-Analysis in Drug Development



John Moss, Stephen Senn, Patrick Fitzgerald and Michael Adena at lunch

Development (1997) and *Dicing With Death* (2003).

Stephen introduced meta-analysis with some basic ideas of how weights can be chosen and various variance formulae. He presented the usual fixed effects approach and a linear model approach, both of which weighted the trials according to internal precision. The methods differed only in the way they estimate the internal precision – globally or locally.

Stephen went on to discuss why meta-analysis is important and observed that many outside the pharmaceutical industry are performing meta-analyses of industry trials and getting them wrong! Stephen produced a quote that reviews should be performed using the Cochrane method and then proceeded to show why this approach is misleading. Many of the attendees were very interested in this discussion as the Cochrane method is the one preferred by the Australian regulatory and reimbursement agencies. Examples were provided that showed the pitfalls of Cochrane's approach to the delight of most of the audience. Stephen was also not very impressed with the software (RevMan) that the Cochrane group and the regulatory authorities require data to be meta-analysed with to the dismay of one of the attendees (who I think had

worked for the Cochrane Collaboration and thought the software excellent).

After giving some of the basic ideas and motivating examples Stephen proceeded to provide some history as a means of introducing more issues. From Karl Pearson's analysis in 1904 in the *BMJ* of inoculation for enteric fever to Juni et al's analysis in 2004 in the *Lancet* of risks of cardiovascular events in taking rofecoxib, meta-analysis has now achieved a century of use and controversy. During this history lesson, Stephen introduced Tippet's approach and even went back to some words from the master – RA Fisher himself – on a test based on the product of probabilities. Stephen talked about the similarities and differences between medical and agricultural research with one very important difference – agricultural research is NOT done by farmers! But, he observes that agricultural research commonly combines data from various sources with things such as main effects and interactions which can be useful when thinking about meta-analyses.

Stephen stressed the differences between the conclusions that could be made using either fixed effects analyses or random effects. Fixed effects are useful when interested in scientific research as opposed to technical research. For example, in scientific research you are interested in the reality

of certain possible phenomena such as 'can this treatment reduce blood pressure'. Whereas in technical research you are interested in more practical questions such as 'will the treatment be useful in practice in typical patients'. Stephen continually came back to these differences throughout the course which was excellent for the attendees as the health economists have been told to produce both approaches when providing submissions for pricing of drugs. Stephen's discussions allowed them to understand why both methods are required and gave them more insight as to which results they wanted to focus on and why.

In addition to providing information on the various methods available for meta-analyses, Stephen ranged over the various global guidelines for drug companies undertaking meta-analyses and the instructions from the Australian regulatory authority on pricing submissions that included meta-analyses giving his insights in his own animated fashion.

Stephen wrapped up the workshop with us working through some case studies. The resulting discussion was very lively, tied all the various approaches together that Stephen had discussed and left participants feeling very satisfied with the workshop.

Caro Badcock

2005 Western Australian Young Statistician's Workshop



Daniel Schubert

The Young Statisticians of the WA branch of the Statistical Society recently held a workshop to promote the statistics industry and statistical careers to young statisticians in Western Australia. The workshop was held on Wednesday 13th July at Tompkins Park, Alfred Cove, where enviable views of the coastline were enjoyed.

The 2005 workshop built upon the aims of the 1994, 1999, 2001 and 2003 workshops to develop, maintain and improve contact and support amongst young statisticians. It was a positive sign for the statistical community in Western Australia to see a turnout of 43 participants – predominantly undergraduates, postgraduates and recent graduates in statistics or related

disciplines. Participants listened to a range of interesting presentations given by invited speakers and other participants. At the end of the day, the young statisticians walked away having

gained a vast amount of information, made new friends and met a number of key professionals in the WA statistical industry.

Our keynote speaker Greg Peterson, from ALCOA Alumina Australia, gave an inspiring talk on how he uses statistics in the production of Alumina. After an introduction to the Alumina production process, Greg explained the importance of his role as an industrial statistician, in making sure a quality controlled product is produced. ALCOA's customers require a high quality product, with the least possible variation. ALCOA Australia was also a major sponsor of the workshop, and it was great to see Greg give such a fantastic presentation.



Joanne Pereira-Gale, Kanchana Perera, Vaike Vohma

Each of our invited speakers was given free reign as to what they talked about, although were asked to focus on the practical side of statistics and its applications to make it more relevant for young statisticians. Some speakers chose to focus on a particular statistical technique that they have used, while others gave a broader perspective of what their career entails. It was interesting to hear about statistical consulting from two different points of view – from a private consulting firm compared to a large government department.

University of Western Australia, Roche, the Telethon Institute for Child Health Research and Murdoch University, makes events such as these possible and we would like to take this opportunity to thank each of them. We would also like to thank all of our speakers for inspiring the next generation of statisticians.

Anna Munday, Pamela McCaskie, April Rutkay



Pamela McCaskie, Jared O'Connell, Ranjodh Singh

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gained a vast amount of information, made new friends and met a number of key professionals in the WA statistical industry.

Young statisticians were also encouraged to present, with a \$200 cash prize available for the best talk. The three Young Statistician speakers presented a range of interesting talks, on topics including 'Stochastic Theories of Income Distribution', 'Detection of Multivariate Outliers', and 'BMI: Better Measure Imminent'. The cash prize (kindly donated by Roche Products) was awarded to Ranjodh Singh from the University of Western Australia for his



Greg Peterson



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Editorial

In the southern states, this mid-winter issue of the newsletter comes at a time of year when the evenings can be cold and wet and the will to attend meetings sometimes drops away. The Branches continue to offer a varied program of talks, and so there is plenty of Branch news in this issue of the newsletter. Newsletter reports remain one of the main ways for Branches to record their activities, and the Editors are always grateful to the meeting correspondents who write up the talks they attend, and to the photographers who help enliven the reports with pictures from the various events.

The American Statistical Association's newsletter is *Amstat News*. A series of articles about the history of statistical societies around the world has been appearing in their newsletter, and in April 2005 the Statistical Society of Australia was featured. A version of the article can be viewed on the SSAI website <http://www.statsoc.org.au/>, through the 'What's New' link.

Finally, this is the last time the August issue of the newsletter will land in your mailbox! From 2006, the publication dates of the newsletter will be February, June, September and December. This aligns the publication of the newsletter with the journal, and moves some of the copy deadlines away from times of the year when many members are difficult to contact. Indeed, the new deadlines for material to be included in the newsletter will be 10 February, 10 May, 10 August and 10 November. The Editors look forward to receiving your material before each of these dates!

ABS Statistical Scholarships awarded in Canberra

On Wednesday 25 May 2005, four actuarial students at the Australian National University (ANU) were awarded an Australian Bureau of Statistics (ABS) Statistical Scholarship. These students were Jessica Twigg and Matthew Carle from second year and Jeffrey Lai and Aiden Hallett from third year.

The ceremony and accompanying lunch were hosted by the School of Finance and Applied Science (FAS) at the ANU, with well over 100 persons in attendance. After introductions by Dr Michael Martin and Professor Terry O'Neill (FAS), the awards were presented by Paul Sutcliffe (ABS). Then, Rebecca Cassidy and Janice Wooton gave short speeches in which they described their experiences as statisticians working within the ABS.

Several ABS Statistical Scholarships are awarded each year by the ABS to students at selected universities who have excelled in statistical subjects in their first and second years. These universities are the University of Adelaide, the University of Wollongong, the University of Queensland, and the ANU. Each scholarship is to the value of \$4000, and is offered for a full year of study in statistics. Application forms for students who wish to apply for the next round can be obtained from the Careers Office or Faculty staff from the relevant universities or by contacting the ABS. The closing date for applications in 2005 is in September. The ABS places no restrictions of future employment on winners of the award.

Borek Puza

President's Corner

The Central Council meeting held in Canberra early in July covered a number of topics that will be of interest to members.

SSAI Review of Statistics

The draft report of the SSAI Review of Statistics at Australian Universities has been available for some weeks (see <http://www.statsoc.org.au/review0405/review.asp> for the link to the report). It is clearly in a draft form and the final version will be polished further but a number of messages come through quite clearly. There is much encouragement for SSAI to take a stronger role in many areas.

Accreditation can be applied in a much broader context than it is currently and the accreditation of courses (including service courses) has set minds to work thinking about the practical aspects.

Recommendations encouraging SSAI to take a more pro-active approach to developing better material for school students and undergraduates are leading us towards providing more useful and interesting material on the SSAI web-site. This could include profiles of some of our members with the aim of highlighting the diversity of vocations that include a solid statistical component. We are looking at some of the materials (including web-sites) already available to students with a view to improving the profile of our profession.

Central Council has strongly endorsed the thrust of the recommendations of the review and is encouraging the Executive to progress initiatives without undue delay caused by waiting up to six months until the next Central Council meeting.

With some funding support from the Australian Research Council (ARC), the Australian Mathematical Society is conducting a review of mathematical sciences in Australia. This will take place early in 2006. The previous review was carried out in 1995 and much has changed since then. SSAI has agreed to contribute \$5,000 to the cost of this review and will assist with the collection of data. We have been closely involved with the establishment of this review and treat it as an opportunity to implement some of the recommendations from the SSAI review.

Structure of SSAI/ASPAI

Having ASPAI (Australian Statistical Publishing Association Incorporated) and SSAI (Statistical Society of Australia Incorporated) as two separate entities causes confusion, with there being two Central Councils, two sets of AGMs, two sets of books and financial reports. Providing clear and comprehensive summaries to the Executive, Central Council, our members and the NZSA (who jointly publish ANZJS with us) is quite a challenge. The use of cash-based reporting has contributed to some recent confusion because the financial year closed at the end of March with SSAI/ASPAI holding about \$100,000 in cash that belonged to Branches (proceeds from workshops) and the SSAI Review. All of our books have been independently audited and there is absolutely no question of there being any improper transactions. The existing summary reports are accurate, but misleading if one is primarily interested in the day-to-day position of the Society. A small team is working with the auditor to move to accrual-based accounting so that financials are reported in a more useful way. These reports will be published in the Newsletter for all to see.

A separate group is looking at the structure of the Society, and will report back with some recommendations. This group is made up of the President, Vice-President, Treasurer, Helen MacGillivray, Murray Jorgensen and Roger Littlejohn. Helen

knows a lot about our existing set-up and the two New Zealanders are part of the team because SSAI and NZSA jointly publish ANZJS.

ASC 2004 – Financial Result

IBC/ASC 2004 financial results have been finalised with SSAI achieving a surplus of \$10,203.47 after returning all of the seed funding. This is

a pleasing result and thanks go to all of those who contributed time and effort to make the conference a success. The lessons learnt along the way are being carried forward to the next few conferences.

Direct Election of SSAI Executive

Central Council has agreed to proceed with the proposal to have one (or more) members of the Executive directly elected by members. Two sets of proposed amendments to the Society rules will be prepared for consideration at the next Central Council meeting in February 2006. The first of these will be to have the President elected via a vote of members. It is envisioned that the nomination process will be similar to the current one and there is no intention to change the fixed two-year term of appointment for President. The second set of amendments will be drafted so that the Secretary and Treasurer will also be elected by a direct vote. For these last two positions, care will need to be taken to ensure that continuity is maintained. It is proposed that members will vote separately on these two sets of amendments at the July 2006 AGM that will be held in Auckland.

New Editor for ANZJS

Congratulations go to Kerrie Mengersen who has been elected as the new Editor of ANZJS. Chris Lloyd has stepped down after more than four years in the role and we congratulate him on the solid contribution that he has made.

New President

My term as President has been completed and Kaye Basford, Professor of Biometry and Head of the School of Land and Food Sciences at The University of Queensland, is now at the helm. Having worked with Kaye during the organisation of IBC/ASC 2004 I am confident that SSAI is in very good hands. I would like to thank all of those who have assisted during the last two years and wish Kaye all the best.

Neville Bartlett

Email: neville@nrbartlett.com.au



**The first issue of the
new electronic journal
BAYESIAN ANALYSIS
has been published at
<http://ba.stat.cmu.edu>**



Hosted By

The Statistical Society of Australia (SSAI) and The New Zealand Statistical Association (NZSA).

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Expression of Interest

If you are interested in attending the Conference, please register your interest on-line www.statsnz2006.com

Scientific Program

A stimulating and cutting edge Scientific Program is being developed to cover a wide range of topics relevant to all statisticians. The program will provide practical knowledge and insights from prominent international and Australasian speakers and will address the latest developments in statistical research, education and practice.

Workshops

Technical workshops that are of particular interest to practitioners will be included in the Conference Program. The Scientific Program Committee is seeking potential workshop presenters. If you are interested in contributing please contact David Scott at d.scott@auckland.ac.nz.

Looking for a job?

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After a small hiatus following visits to Canada and Australia in the 2004 SSAI newsletters our journey continues into Europe. A/Prof Gita Mishra is a senior research fellow for the Medical Research Council – National Survey of Health and Development at the Royal Free & University College, London Medical School as well as a conjoint senior research fellow with the University of Queensland. As a senior biostatistician, Gita has been researching new methods to analyse and report on human nutrition studies.

A brief journey around the globe Statistics and Nutrition Research in the UK

Like other nations, Britain is experiencing many public health issues associated with the demographic changes of an ageing population and rising levels of obesity which are likely to create further demands on stretched health resources. As a result the government has started to recognise the substantial benefits of research in areas such as nutritional epidemiology in providing information to assist with policy development, allocation of resources, and targeting health initiatives more effectively.

It is also the case that nutrition, at least in terms of dietary advice, is of great public interest. Particularly since this country has endured numerous 'food scares' in recent years and where the media constantly publicise the latest dietary fad, as well as conflicting and confusing messages about risks associated with the consumption of specific foods. Sudden shifts in dietary patterns in response to a new regime, for instance by avoiding foods high in carbohydrates, can have uncertain long-term health consequences for the individual and damaging economic consequences for food producers at the national level as well.

Into this culturally, economically, and politically charged ring the statistician must step to provide the kind of clarity to dietary data that can allow appropriate health policy and guidelines to be developed. The real challenge for the statistician is that dietary data and the resultant nutrient intakes are notoriously prone to error

and bias. For instance, the nutritional benefit from an individual food item may vary considerably according to its freshness, the storage system, and method of preparation, as well as the type of accompanying foods. The high degree of interest in the topic means that surveys on food intake are often biased. Anyone who has completed a food diary can attest to the temptation to overlook certain 'unhealthy' items. Some people even report consumption levels that convert into caloric intakes below that required for physical survival!

Most research has concentrated on effects of current diet and has tended to apply straightforward analysis techniques. An area of recent interest concerns life course nutrition and the role of diet at specific periods, such as early childhood, on health outcomes in later life. Longitudinal studies over the time span required are expensive and difficult to maintain so one of the main methodological challenges has been to find ways of shedding new light on data from existing studies through analyses that address more complex relationships, such as investigating diet and health trajectories. In addition, attention is being paid to techniques that better account for bias and measurement error, for instance Bayesian techniques that use 'prior knowledge' to reduce measurement error and multiple imputation to reduce the effect of missing values that are biased.

The next major development appears to be the arrival of genomics and the possibility of investigating the relationship between genetic and environmental effects, such as when a specific genetic inheritance may make an individual more susceptible to the impact of certain dietary patterns. Whatever may be said about statistics in nutrition research, with the many new avenues of research opening up and the demand for actionable results, the future will certainly be far from dull.

by A/Prof Gita Mishra.

I look forward to providing further reports of statistical research in the medical sciences from colleagues around the world and hope that readers are finding them of interest.

Peter Howley

Conferences

Fifth International Symposium on Business and Industrial Statistics

11-13 January 2006, Lima, Peru
www.stat.vt.edu/isbis5

ASC/NZSA 2006 Statistical Connections

3-7 July 2006, Auckland, New Zealand. www.statsnz2006.com

ISI2007, Lisbon, Portugal
<http://www.ine.pt>



Selected highlights from ISI 2005

Welcome to ISI

The 55th Session of the International Statistical Institute (ISI) was opened by the Australian Parliamentary Secretary to the Treasurer, The Hon. Chris Pearce, MP.



In his wide-ranging speech, the Parliamentary Secretary praised the work of statisticians because they helped people and governments to understand the world they lived in and plan more effectively for the future.

“Without access to well-founded statistics, mankind is unlikely to fulfil its collective dreams of a better world,” he said.

“You statisticians give us the tools to take a hard look at ourselves, to see where we stand, how we arrived there, and to make informed decisions about how to proceed into the future.

“There can be no doubt that today governments, corporations and communities increasingly rely on data, not only to achieve their immediate aims, but often for their very survival.

“It is obvious that unless we have the skilled statisticians to provide quality data, and unless those statisticians are developing and maintaining the highest professional standards, the path into the future could be foggy indeed.”

Using the ABS as an example, Mr Pearce said that national statistical

offices represented a vast warehouse of knowledge on people and society.

“It enables us to have a good look at ourselves, statistically speaking,” he said.

“If we don’t like what we see, we have the opportunity to apply treatments, often in the way of policy interventions, to improve the image we see.”

He said that national statistical offices could provide a vital resource to their governments and their communities, but only if the statistics were treated seriously. Successive Australian Governments had given their full support to the ABS, regardless of their political persuasion because they trusted the work of the agency.

At the heart of the trust placed in the organisation was the influence of core values on the way the ABS conducts itself.

“These values, which have remained constant during the Bureau’s history, can be summed up as relevance, integrity, professionalism, equality of access to data, and protection of the confidentiality of information provided to the Bureau by both individuals and organisations,” he said.

“The ABS can build on its record over the past 100 years to continue its contribution to informed decision-making, research and discussion, well into Australia’s future.”

History of Statistical Globalisation

At the opening ceremony, the President of the ISI, Stephen Stigler, traced the global development of statistics by citing two key figures central to the statistical history of Australia.

“I will be content to do what statisticians usually do and sample, invoking two historical figures as representative symbols of that history and the globalisation I mention,” he said.

“This sample is not a random one, the two individuals both have deep intellectual roots in Sydney.”

The first of these key Australians was William Stanley Jevons, who contributed importantly to the early development of the Australian statistical system.



“His international travel and Sydney residence had an immense effect on the development of his thought and work,” he said.

Stephen’s second example was George Handley Knibbs, the first Commonwealth Statistician.

Knibbs brought a “new global perspective” to his office, being elected to ISI in 1913 and regularly visiting other statistical bureaus.

In summing up, Stephen said: “Both returned from their journeys with intellectual treasure, and others followed, as we do today.”

Trust First and Foremost

Dennis Trewin, as the chair of the National Organising Committee, also spoke at the opening ceremony. Dennis highlighted that this Session of the ISI brought some new elements into the structure of the ISI program, the most notable of these being the introduction of theme days.

Theme days - on the environment, financial statistics and genomics - have been introduced to give non-statistical professionals working in these fields the opportunity to attend a full day of

relevant sessions and be introduced to, and network with, statistical experts.

In keeping with the centenary year of the ABS, Dennis touched on the importance of understanding an organisation's history in planning for the future. He also noted that a common topic of major importance to statistical agencies worldwide was trust, echoing the comments from The Hon. Chris Pearce, MP.

Dennis went on to highlight the emerging roles that a national statistical office will have to take on, as the world of statistics is changing and moving towards a system where the national statistical office is only one of many providers of statistics.

Dennis argued that statistical leadership is needed across all statistics that are of national importance, and that statistical offices are well placed if they are willing to take the initiative in this area.

Official statisticians had to be prepared to talk and engage with the people who provide data and use statistical services, and not just talk among themselves.

The full text of the opening speeches from ISI200 can be found at <http://www.tourhosts.com.au/isi2005/media.asp>

A Statistically Significant Shortage

"The biotechnology revolution is creating huge opportunities for statisticians," says Dr David Mitchell, who originally trained in biological sciences and now heads a group of bioinformaticians and statisticians at CSIRO Mathematical and Information Sciences.



"Understanding the kind of data being generated in biotechnology today requires quite different types of statistical analyses from those used in biological sciences in the past," he says.

"However, most biological scientists today are not trained in statistics and thus do not have the skills required to analyse this data," he says.

"The main problem is the greatly reduced capacity of our schools and universities to train professionals in the mathematical and statistical sciences," says Professor Peter Hall of the Mathematical Sciences Institute, Australian National University. "For example, the number of mathematicians working in our universities today is almost 40% fewer than it was a decade ago."

During 2003, just over 3,000 PhDs were awarded in Australia in the natural and physical sciences. Of these almost half were in the biological sciences while only 186 were in the mathematical and statistical sciences.

"Combined with the low number of people studying statistics, this has created both an enormous shortage of good statisticians to do the work, and a lack of critical mass in Australia to develop new technologies," says Dr Mitchell.

"The worst-case scenario is that Australia will fail to capitalise on opportunities in fields like drug discovery and novel diagnostics because we don't have research statisticians to develop the new approaches to data analysis that are required," he says.

Dr Mitchell's team at CSIRO is developing new statistical methods to deal with the new kind of biotechnology data. Their methods are enabling them to develop simpler ways to diagnose diseases like leukaemia and to identify plant genes that are of commercial importance in agriculture.

The team now plans to use their new statistical methods to tackle systems biology, which means understanding how a whole organism works, rather than its individual parts.

A match made by statistics - Florence Nightingale and Casanova

What do Florence Nightingale and Casanova have in common? Although

history's records place them as polar opposites, the truth is that they were both statisticians.

History records Florence Nightingale as pioneering the nursing profession and discovering that poor sanitation caused death.

In 1854, she was recruited to serve as a military nurse during the Crimean war. During this time, in one of history's little known facts, Florence Nightingale collected data on mortality rates and pioneered a new statistical analysis called the "polar area diagram" to plot the incidence of preventable deaths.

Her charts and graphs showed that improving sanitary methods saved lives. Her calculations proved to be true because as soon as her sanitary reforms were implemented the mortality rate dropped.

In 1856 Florence Nightingale was made a Fellow of the Royal Statistical Society.

On the other hand, Casanova's reputation as a lover and an adventurer is widely known. But his gambling and his institution of the Casanova's lottery, which was drawn in France for 78 years, are not well recognised.

Thanks to a published paper by ISI President, Stephen Stigler, we know that in 1756, when Casanova was asked by French King Louis XV's mistress, Madame de Pompadour, for suggestions on how to raise money for the King's military school, he proposed a lottery.

With the concept of a lottery unknown in France at the time, Casanova needed to convince the King's state council that the lottery would not produce a major loss.

Casanova advocated his idea at two hearings of the state council and he offered to prove the soundness of his lottery before all the mathematicians in Europe. After intense scrutiny, the King backed the lottery.

Casanova's lottery proved to be a phenomenal success.

The lottery continued growing with more frequent draws and tickets on sale in regional France, until 78 years later when the moralists of the day stopped it in 1836.

Stephen has analysed Casanova's lottery and says that it was "remarkably fair." *Continued over the page*



Denise Lievesley - ISI President-elect

Denise Lievesley has become the first woman to be President-elect in the 152-year history of the ISI meetings. She will assume the Presidency in 2007, for the standard two-year term.

"I feel humble, but honoured by being President-elect," she said.

"During my time in office I hope to establish better links both amongst the various national societies and with the ISI.

"In particular I am keen to use such links to improve support of statistical societies in the developing world as a way to help improve the condition of some of the world's less fortunate nations.

"I'm an active reformer and am keen to look at strategic changes that can make a difference for the ISI. There are some issues ahead of us to consider, such as the future of the associations, the cost of meetings and the financial implications of changing from printed to online information.

"We also have to think about recruitment and training of statisticians and ways to encourage increased integrity in official statistics so that there is an appropriate balance between policy relevance and political independence."

Denise has had a lifetime love of mathematics and is presently Director of Statistics at UNESCO. A social statistician by training, she has also been Director of the ISI, President of the International Association for Official Statistics and elected Fellow of the ASA.

Three Doors

Three Doors with Borek Puza (Edition 3)

Welcome to the third edition of *Three Doors*. In the last edition we presented The Sample Size Puzzle. This time I am pleased to announce that Terry Neeman's very elegant solution has won her a dinner voucher worth \$60, as donated by the SSAI. Below is the puzzle, its solutions and a discussion. The next puzzle follows.

The Sample Size Puzzle

Consider a random sample of n values from the normal distribution with mean k and variance 1. Suppose that n had previously been obtained by flipping a coin and taking n as 1 if tails came up and as 2 if heads came up. Also suppose that k is assigned an improper flat prior distribution over the whole real line, independently of n . We now observe that the total of the n values is 1.000. Find the probability that $n = 1$.

Solution to The Sample Size Puzzle

Let t be the total of the n values, and let $f(x)$ stand generally for the probability density or mass function of x . Then $(t|k,n) \sim N(nk,n)$, where $f(n) = 1/2$, $n = 1,2$, and $f(k|n)$ is proportional to 1 for all k in the real line. Our task is to find the posterior probability $q = P(n = 1 | t = 1)$. Now, $f(n|t)$ is proportional to $f(n,t)$, which equals the integral from minus infinity to infinity of $f(n,t,k) = f(n)f(k|n)f(t|k,n)$ with respect to k . It is easy to show that this integral is proportional to $1/n$. Hence $q = (1/1) / \{(1/1) + (1/2)\} = 2/3$.

Discussion

Our inference implies that the sample is *twice* as likely to contain one observation as it is to contain two. But there are two problems with this. First, it seems rather odd that knowledge about t should influence our beliefs regarding n . Secondly, observe that $f(n|t)$ does not depend on t , since nowhere have we made use of the fact that $t = 1$. (We would have got exactly the same result if t had been 274, say.) Hence $f(n|t)$ must be the same as $f(n)$, and therefore $q = P(n = 1) = 1/2$, not $2/3$. What is going on here?

This paradox is due to the improper prior on k . If instead we take $(k|n) \sim N(0,v)$, where v is large but finite, we find that $f(n|t)$ *does* depend on t . However, as v tends to infinity, the dependence diminishes and q approaches $2/3$. This goes to show that a flat prior over the whole real line, or a proper prior approximating it, is not always uninformative. For more details see Puza, Brewer and O'Neill (2005).

The Nine Number Puzzle

You are about to play a game in which 9 numbers will be randomly drawn from between 0 and 1 (uniformly, independently, and one by one). Just after observing each number, you must either accept or reject it, but you may accept only once. The accepted number will be multiplied by 1000 and you will win that number of dollars. Find your maximum expected gain and describe the corresponding optimal strategy.

For your chance to win a fabulous mystery prize, send your solution (sooner rather than later) to <borek.puza@anu.edu.au>.

References

Puza, B.D., Brewer, K.R.W., and O'Neill, T.J. (2005). Another posterior paradox.

The Mathematical Scientist, 30(1), 33-42.

The Third Sir Roland Wilson Lecture by Dennis Trewin

On Wednesday 1 June 2005 the 13th Australian Statistician (AS), Mr Dennis Trewin, presented the Third Sir Roland Wilson Lecture, titled '100 Years of Official Statistics'. The venue was the APSEG (Asia Pacific School of Economics and Government) Lecture Theatre in the Sir Roland Wilson Building at the Australian National University (ANU), Canberra, and the host was the Chair of the Sir Roland Wilson Foundation and past Vice-Chancellor of the ANU, Emeritus Professor Deane Terrell, AO. Deane introduced Dennis by mentioning that he has been the AS since 2000, was previously Deputy AS, was Deputy Government Statistician in New Zealand from 1992 to 1995, and currently holds several other senior appointments in Australia, such as Adjunct Professor at Swinburne University and Electoral Commissioner.

Dennis began by describing the pre-Federation days in Australia (before 1901) when each colony had an autonomous statistical office, some of which were world class. The *Census and Statistics Act 1905* was prompted by a need for national statistics and national standards which became apparent from the many comparability problems in the 1901 Population Census. The Act created the office of Commonwealth Statistician (CS) and invested its holder with the authority to conduct statistical collections and, when necessary, to direct a person to provide statistical information. The Act also resulted in the creation of the Commonwealth Bureau of Census and Statistics (CBCS).

The first CS was George Handley Knibbs, a first class demographer who was appointed in 1906, and the CBCS initially consisted of only 12 persons. During the period from 1905 to 1924 the CBCS took on ever increasing responsibilities, with conferences of state premiers in 1906, 1918 and 1923 passing resolutions in favour of combining Commonwealth and State Bureaus. Tasmania agreed to join the Commonwealth Bureau in 1924, mainly

for economic reasons. This led to a succession of CS's of Tasmanian origin, such as L.F. Giblin, E.T. McPhee, R. Wilson, K.M. Archer and J.P. O'Neill, whose combined length of service in that role was about 50 years.

From 1924 to 1956 the remaining state bureaus all integrated into the CBCS. The CS's during this period were C.H. Wickens, L.F. Giblin, E.T. McPhee, R. Wilson and S. Carver. As CS, Roland Wilson developed the balance of payments, a range of business statistics and production indexes and coordinated a major upgrade of retail price indexes. He also invented the position of 'Research Officer', which allowed graduates to enter the Australian Public Service (APS) on the basis of their university qualifications. Previously, graduates could enter only as base grade clerks, unless they held professional qualifications such as medical or engineering degrees. Wilson also initiated overseas scholarships for public service graduates and sent out scouts around universities to find promising young people. Such innovations contributed to the strong international reputation of the CBCS. Wilson was also the first to appoint a female librarian in the APS, and later wrote: 'I picked her out first and then made up the selection criteria so that she would win. She won hands down'. Dennis also related an amusing anecdote regarding Wilson and a Commissioner of Taxation which can be found on page 2 of the May 2005 issue of the SSAI Newsletter (Number 111).

The period from 1956 to 1975 was marked by a strong growth in statistical output and size of the CBCS. It also saw an increase in research and development and a widespread introduction of sample surveys, particularly due to the work of Ken Foreman. These were the early days of computing, and the CBCS was one of the first public sector organisations in Australia to use a mainframe computer. The CS's during this period were S. Carver, K. Archer, and J.P. O'Neill.

In 1974 the Committee on Integration of Data Systems (or the Crisp Committee) recommended wide-ranging reforms, and this led to the *Australian Bureau of Statistics (ABS) Act 1975* and subsequently to the creation of the ABS itself. Thus the ABS was born from the CBCS in 1975 as an independent statutory authority with well defined functions, responsibilities and rights. In particular, the ABS was given a political autonomy which has so far been respected by both major political parties, but not enshrined in legislation. The Act also created the position of Australian Statistician to become head of the organisation, replacing the former position of Commonwealth Statistician.

Since 1975 the ABS has seen many significant developments, including a greater flexibility in the release of statistics, for example by way of microdata, CD ROM's and website pages, and a much stronger corporate focus and client orientation. The latter was helped by the introduction of 'user pays', although not all users appreciated the need to pay! There has also been a rapid expansion of social statistics, mainly as a consequence of the household survey program, and the introduction of more analysis to assist the interpretation of statistics. The AS's during this latter period were Jack O'Neill, Roy Cameron, Ian Castles (in the audience) and Bill McLennan. For the future of the ABS, Dennis sees an increasing reliance on administrative and transactional data bases, a greater use of analytical and model based methods, the availability of more 'granular' data, and more extensive and consistent international comparisons. He is confident that the ABS will continue in its role as a strong statistical leader, both nationally and internationally.

Borek Puza
12 June 2005

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Professional Development Opportunities by SSAI

Symposium on Data Linkage – September 6th, ANU Campus, Canberra

Data linkage is an important and rapidly growing area. It involves bringing together data from different sources in order to enable improved, and often otherwise unavailable, insights to be drawn from the combined data set. Linked data sets can often address key research questions or assist policy and planning. For instance, they may provide an understanding of the patterns of use between different services or treatments, monitor the effects of one type of service on another or help identify trends in outcomes over time.

This one day symposium will raise key issues for consideration and discussion concerning the appropriate design and conduct of data linkage projects. Our invited speakers from the Australian National University (ANU), Australian Institute of Health and Welfare (AIHW), National Centre for Epidemiology and Public Health (NCEPH), CSIRO and ABS will cover a range of diverse topics that arise in data linkage projects, from preserving confidentiality and data linkage strategies, to realising the powerful potential of combining information and understanding the limitations of linked data sets. An opportunity for open discussion will follow the talks.

Registration details are available at the Canberra branch website: <http://www.statsoc.org.au/Branches/Canberra/DataLinkageSymposium.pdf> or contact Terry Neeman (terry.neeman@gmail.com) for any additional information.

Bayesian Retreat – ‘Topics in the Tropics’ – 28-30 September 2005, Stradbroke Island, Qld

The Bayesian Retreat, ‘Topics in the Tropics’, is our second annual joint meeting of the Australasian Society for Bayesian Analysis (a section of ISBA; see <http://www.bayesian.org/>) and the Statistical Society of Australia’s Section on Bayesian Analysis (see <http://www.statsoc.org.au/>). The meeting is held in the same location as last year: beautiful Stradbroke Island. The aim is to bring together researchers and practitioners with a common interest in the methodology and application of Bayesian data analysis. The meeting is intentionally small and friendly, with a focus on active discussion and participation among all attendees. The programme includes keynote addresses, detailed case studies of Bayesian analysis in practice, and hands-on workshops. This year, our international keynote speaker is Robert Wolpert, Professor of Statistics at Duke University in the USA: see his webpage at <http://www.stat.duke.edu/~rlw/>.

Registration info at www.statsoc.org.au/cpd/BayesOSInfo&Registration.pdf

Professional Development Opportunities

Bayes for Beginners Workshop – 4 & 5 October, Adelaide University Campus

The South Australian Branch will conduct a workshop on ‘Bayes for Beginners’. The workshop will be presented by Kerrie Mengersen, an active researcher in Bayesian statistics and an experienced facilitator of short courses in this field. It is designed as an introduction to the concepts and methods underlying Bayesian data analysis and the package Win-BUGS (a freeware package for Bayesian analysis) will be introduced. No experience with Bayesian analysis is assumed, however an understanding of basic statistics is essential. More details will be made available shortly on the SSAI website. Registration information is available at: <http://www.statsoc.org.au/CPD/SAYBAYS2005Regn&Info.pdf>

Short Course

Spacial Analysis in Environmental Epidemiology

5-8 September 2005, Canberra

http://nceph.anu.edu.au/Envir_Collab/Short_Courses/index.php

Branch Reports

WESTERN AUSTRALIA

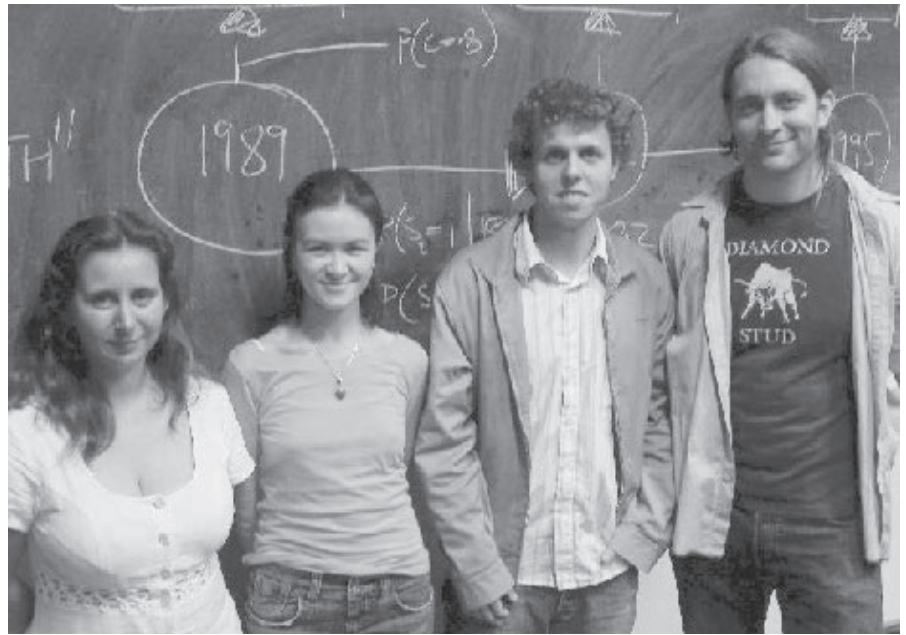
May 2005

The WA Branch of the SSAI enjoyed a wonderful evening with young statisticians at their May Branch meeting. To begin the evening, Anna Hepworth from Murdoch University was presented with the 2005 SSAI Honours Scholarship Prize which included student membership to the society. Anna, a mother of three, is currently completing an honours degree in statistics, researching 'Principal component analysis for data with missing values' to add to her Bachelor of Science with Honours in Psychology. The calibre of applicants for the scholarship was so high this year that the WA Branch committee decided to award a second student SSAI membership to another outstanding applicant, Vaike Vohma of Murdoch University.

The evening continued with two young statisticians presenting talks discussing their current area of work.

Jared O'Connell, last year's Honours Scholarship recipient and currently working with the CSIRO in Perth, began the seminar part of the evening and spoke about 'Estimating Land-Cover Change' in Australia over the last thirty years. The Land-Cover change project involves classifying land cover into two categories; greater than 20% tall woody vegetation and less than 20% tall woody vegetation in order to identify the time and location of land cover change. One step in this analysis involves applying conditional probability networks (CPNs) to classified satellite imagery. This technique integrates spatial and temporal information with the original classifications yielding great improvements in the accuracy of land-cover estimates. The cost of these improvements is that a CPN analysis typically takes 3 to 7 days to run. Jared discussed how he increased the speed of the CPN by a factor of twelve via the implementation of a parallel version of the CPN software.

The second talk of the evening was given by Rohan Sadler, a PhD student working jointly with the school of Agriculture and the school of Mathematics and Statistics at the University of Western Australia. The two talks complemented each other well, with Rohan discussing his current research into 'Fitting Ecological Knowledge to Remotely Sensed Imagery'. Remotely sensed imagery is becoming increasingly available as a



(L to R) Anna Hepworth (winner of SSAI Honours scholarship), Vaike Vohma (special commendation of SSAI Honours scholarship), Jared O'Connell (YS speaker) and Rohan Sadler (YS speaker).

resource in understanding vegetation patterns. Rohan's research is interested in how these patterns are formed over time, the stability of vegetation pattern dynamics as an indicator or ecosystem resilience, and how patterns are driven by complex interactions of events such as fire and rainfall. Types of statistical tools that can be used for understanding vegetable dynamics include spatial point process, grid-based and ad hoc models. Point process models rely on precise information about point locations, and this information is not easily obtained from remotely sensed images. Rohan is developing a methodology to fit ad hoc models of ecological knowledge for a time series of image data captured from the long-term monitoring of *Themeda triandra* (Kangaroo grass) grasslands in the Pilbara region of Western Australia.

After the seminars, a number of branch members went to a local restaurant for dinner with the two speakers. The evening provided a wonderful opportunity for some of our newest members to see how a statistician can apply their knowledge and to interact with young and not-so-young statisticians alike.

Pamela McCaskie

June 2005

Members' preconceptions were challenged by Dr Ross Taplin's (Murdoch University) title *Teaching Statistical Consulting: A debate about the Statistics profession*. Ross teaches consulting

courses to university students who have taken only an introductory first-year statistics unit, and even to students with no knowledge of inferential techniques. Ross began by posing the question: What is (applied) Statistics? Audience discussion was stimulated by quotes of some consulting gurus, as well as some views on statistical education. For example, David Moore echoing a longer statement issued by the National Research Council, writes 'In practice, the new pedagogy asks us to change what students do from listening and reading to active participation'.

Active participation was illustrated with a short interlude of rôle-play in which members paired off with one member playing the part of a client seeking a quick answer from the other, the consultant. The client read a short statement, for example (and paraphrasing), 'My AFL coach says I should kick rather than handball. He calculates a correlation coefficient 0.58 between the average number of kicks per quarter and the average number of goals per game of 20 full-forwards. He says his opinion is sound because $0.58 > 0.5$. I think this comparison is unfair because kicks per quarter is compared with goals per game. Shouldn't he calculate the correlation coefficient with both averages per game to see if this is bigger than 0.5?' The client had further background information which the consultant could elicit with appropriate questions, and then try to give appropriate advice. One

issue here is recognizing the tension between correlation and causation. Rôles were reversed for another play.

Members were asked for impressions and comments, provoked by more quotes. Moore again: '... statistics is not a subfield of mathematics, and that in consequence, beginning instruction that is primarily mathematical, or even structured according to underlying mathematical theory, is misguided'. Discussion of the use of student projects was introduced with opposing quotes such as 'The project is motivating, and gives students a feeling of working in an almost real-life environment on a real problem' contrasting with, 'Projects in schools are little more than collections of calculations and charts which may gain points but show no underlying statistical coherence'.

Ross teaches consulting to second-year university students who have completed a first-year introductory statistics unit and who volunteer to participate. They attend twelve one-hour classes and engage in rôle-plays as an introduction to consulting with real clients. He finds that many students are initially scared but become more confident as the play evolves, and look forward to more rôle-plays. They enjoy using their knowledge to help others, but have difficulty remembering and applying this knowledge. Some find it hard to communicate orally, but appreciate its value. Students gain understanding of statistics as a profession.

Ross has conducted rôle-play classes with 150 Year-12 students taking Applicable Mathematics (matrix algebra, probability and statistics). Sessions lasted from 35 to 55 minutes, and included a brief introduction to the statistics profession, two dummy rôle-plays and two real ones. Outcomes were assessed using pre- and post-class surveys. The pre-survey included the statements (with percentages in agreement): Statistics is useful (69%); Statistics is boring (34%); I am good with numbers (84%); I am good with people (50%); I would consider working as a statistician (16%); My career will involve statistics (37%). The post-survey showed very little change, the largest being a 0.7% reduction in 'good with numbers' and a 0.7% increase in 'good with people'. All but the second showed a small increase. More encouraging, the post-survey included the following statements (with percentages for and against): I enjoyed the rôle-plays (65%, 17%); They were helpful for learning statistics (70%, 14%); I learnt

about the work of statisticians (86%, 4%); I preferred the rôle of consultant (36%, 35%); I communicated ideas correctly (23%, 29%). Ross observed that in general these students didn't correctly apply statistical knowledge in their rôle-plays, e.g., recognizing a lower quartile.

Some 50 high-school teachers participated in rôle-plays at a professional development evening. Eighteen of them completed a voluntary survey. These respondents all agreed that rôle-plays were fun and helpful for learning statistics, and that they would use them in their teaching.

Ross emphasized that he uses rôle-plays at secondary and early tertiary level *not* as a recruiting device but rather to improve learning outcomes and to raise awareness of statistics as a profession. He believes these aims are achieved, and that students enjoy the experience, that rôle-plays encourage positive attitudes, and that they are easy to implement. Some disadvantages he mentioned are that rôle-plays take time from other modes of instruction, some students may be discouraged or not take them seriously, they are not real work-experience, and that they are not examinable.

Discussion opened with two short presentations. Pam McCaskie, a PhD scholar recently graduated with majors in human biology and applied statistics, spoke of the value she derived from the UWA applied statistics major, and opined upon why graduates in statistics don't become school teachers. Dr John Henstridge commented from his standpoint as managing director of a substantial consulting firm. He drew a contrast between teaching consulting for its own sake, and consulting teaching to heighten interest in statistics. Working consultants need maturity in the discipline, so teaching consulting should begin near the postgraduate level. In addition, contrary to Moore's opinions, mathematics and statistics *do* go together at the university level. John cited (with approval?) the U.K. Smith Report which recommends that if any mathematics topics are to be dropped from the school syllabus, then statistics should be the first to go. On the other hand, he commended Ross' rôle-plays as a valuable adjunct to statistics teaching at secondary and early tertiary levels.

The meeting was thrown open to general discussion which continued over dinner at a local eatery.

Tony Pakes

CANBERRA

Improving confidence intervals via tail functions

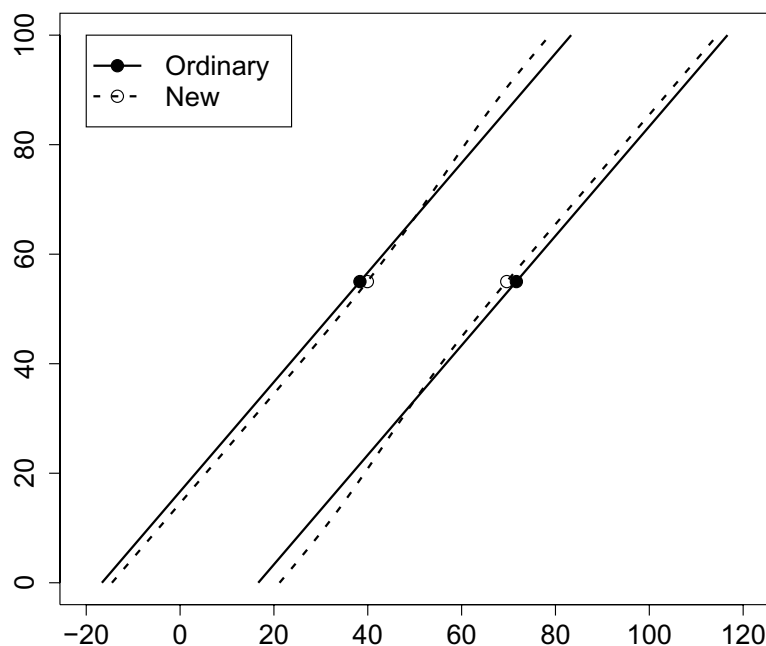
At the monthly meeting of the Canberra Branch of the SSAI on Tuesday 26 April 2005, Dr Borek Puza of the School of Finance and Applied Statistics (FAS) at the Australian National University presented a lecture titled 'Improving confidence intervals *via* tail functions'. This lecture was an expanded version of a talk on the same topic which Borek recently gave at the 55th Session of the International Statistical Institute (ISI) (Sydney, 5-12 April 2005). Both presentations were based on joint research with Professor Terry O'Neill (FAS) which is on track for publication in the *Journal of Statistical Computation and Simulation* and the *Canadian Journal of Statistics*. A technical report will soon be made available at <http://ecocomm.anu.edu.au/research/papers/papers.asp?disc=STAT>

The classical theory of interval estimation involves inverting a probability statement regarding a pivotal quantity so as to obtain a confidence interval (CI) which contains the target parameter with the desired level (e.g. 95%). This theory requires that equal areas (e.g. 2.5%) be 'cut off' from either tail of the pivotal quantity's distribution. The new methodology involves specifying these areas in terms of a function of the parameter, called the *tail function*, and proceeding to invert the probability statement as before. The result is a new CI whose bounds can be calculated by solving two equations *via* the Newton Raphson algorithm.

This approach can be used to shorten CI's when prior information is available. By contrast, the Bayesian approach can lead to even shorter intervals (such as the highest posterior density region) which however do not have the desired coverage probability for all possible parameter values. Thus, the tail function methodology provides an attractive alternative to the Bayesian paradigm when prior information is available and a proper frequentist CI is required.

To illustrate, the solid lines in the figure below represent the lower and upper bounds of the ordinary 95% CI for a normal mean (horizontal axis) for all possible values of the sample mean from 0 to 100 (vertical axis), when a sample of size 4 has been drawn from a normal distribution with variance 289.

The dashed lines show the new 95% CI based on a particular tail function. For example, if the sample mean is 55 then the ordinary 95% CI is (38.3, 71.7) (dots) and the new 95% CI is (39.9, 69.6) (circles). In this case the tail function methodology has resulted in a width reduction of about 11%.



Observe that the new CI is shorter than the ordinary one for values of the sample mean near 50 and wider for values far from 50. Thus, if the prior distribution of the normal mean is concentrated near 50 then the prior expected length of the new CI will be less than that of the ordinary one (33.4). A reasonable strategy is to define a broad class of tail functions and search for the member of that class which provides a CI with the smallest possible prior expected length.

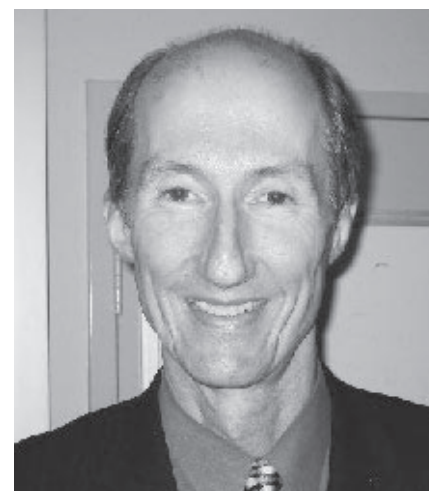
It should be kept in mind that narrowing a CI in this way comes with the risk that the interval may end up being *wider*. This can happen if the prior has been misspecified or the data are by chance extreme. Thus the use of tail functions involves an element of gambling. But the danger can be controlled by restricting the search for an optimal tail function within a subclass for which the maximum width of the new CI is set at an acceptable level. Ideally, the tail function should be decided on *before* the data have been observed. Otherwise there may be an inflated coverage effect. Note that this advice applies equally to *any* situation where a choice needs to be made between two or more CI's.

Tail functions also have applications other than the shortening of CI's. For example, they can be used to improve the coverage properties of approximate CI's for parameters of discrete distributions (such as the binomial) and to fix the problem of a randomised CI possibly being empty.

Experiences of a statistician in the pharmaceutical industry by Philip McCloud

At the monthly meeting of the Canberra Branch of the SSAI on Tuesday 31 May 2005 Dr Philip McCloud of Roche Products Pty Ltd, the Australian Affiliate of Hoffman La Roche, gave a talk titled 'Some Statistical Experiences from the Pharmaceutical Industry'. Philip graduated with a degree in statistics from Flinders University in 1975 and lectured at Monash University from 1989 to 1997. In 1997 he joined Roche in Sydney, where he is currently Head of Biostatistics. The Roche Group employs about 70,000 people in 100 countries, including 700 in Australia.

Philip began by giving a very illuminating overview of the strategic life cycle of a pharmaceutical drug. Only about 1 in every 10,000 chemicals tested makes it to the market. The process from the discovery of a successful drug to its release onto the market typically takes about 10 years, costs several hundred million dollars, and contains a number of clinical trials, including a Phase II trial to determine the optimal dose and a Phase III trial for comparison with standard treatments. Once the drug has



Philip McCloud

been approved, it earns anything from a few hundred million dollars a year to two billion dollars per year for a real blockbuster. For example, MabThera (a top Roche product) cost US\$800 million to develop and is currently generating sales of 2 billion Swiss francs per year worldwide.

Biostatisticians in the pharmaceutical industry are principally responsible for the design and analysis of clinical trials. Philip has been the Project Statistician for the development of Pegasys (pegylated interferon) in the treatment of hepatitis B. Pegasys was already an approved treatment for hepatitis C and has the advantage of requiring one injection a week compared to three with conventional interferon. The Phase III study in hepatitis B positive disease recruited 270 patients in each of three treatment groups (including the comparator called Lamivudine), lasted 72 weeks (including 24 weeks of followup), and has resulted in the approval of Pegasys for the treatment of hepatitis B in over 40 countries, including Switzerland, China and America. The USFDA (United States Food and Drug Administration) approved it on 13 May 2005.

In Australia the listing of drugs on the PBS (Pharmaceutical Benefits Scheme) is often based on cost minimisation. The Incremental Cost Effectiveness Ratio (ICER) is one of the measures used to justify the price for a new drug. It is defined as the total cost of the drug minus the total cost of a comparator drug all divided by the life expectancy of a patient using the drug minus the life expectancy of a patient using the comparator drug. Thus the ICER represents the extra cost of the drug for every year of additional life. Philip showed how the delta method can be used to provide a confidence

interval for the ICER for Pegasys relative to Rebetrone (a conventional interferon) which is narrower than the one previously obtained using cruder methods. The calculation of the shorter interval was part of the process which eventually led to Pegasys being listed on the PBS for the treatment of hepatitis C.

Philip described the construction of control charts for assessing whether patients are being recruited into a study at an appropriate rate. Philip showed how he has used the negative binomial distribution to model the variation in patient numbers. He then showed some control charts which he designed for monitoring the recruitment of patients into a global metastatic gastric cancer study. These charts have assisted the Global Head of the Operations Department at Roche to assess whether recruitment into this study is too slow and to then decide on appropriate courses of action, such as initiating additional medical sites.

Philip concluded his presentation by discussing unrecognised adverse events, citing the example of Vioxx, a drug for rheumatoid arthritis which featured recently on the Four Corners programme (ABC TV). Vioxx was approved by the USFDA in 1999 but recalled in 2004 after studies showed that it doubles or triples the risk of heart attack or stroke. The database for the new drug application contained over 500 patients and did not show an increased risk of thrombotic events, although treatment was for only six months. The year after approval, the VIGOR study reported patients receiving 50 mg Vioxx had a 2.36 increased risk of a thrombotic event compared to the comparator group who received Naproxen; the median length of followup was 10.5 months. Merck argued that the increased risk was because Naproxen was protective against thrombotic events. Some clinicians questioned this reasoning, claiming that the protective effect would be no greater than 30-40%. Finally the APPROVe study reported a 1.96 increase in the risk of thrombotic events with 25mg of Vioxx compared to placebo. Previously the lower dose of 25mg had appeared to be completely safe. In fact the results for the first 18 months did not show an increased risk of confirmed thrombotic events. The increased risk was only observed after 18 months of treatment. The dilemma that faces society and the pharmaceutical industry is how to deliver efficacious drugs to the patients who need them in the shortest time without compromising safety. An improved system of post-

approval monitoring for adverse events is required.

Borek Puza

SOUTH AUSTRALIA

Interaction in factorial experiments may be the result of additivity plus nonlinearity, and statisticians need to tell their clients this

The June meeting of the SA branch was addressed by Dr. Paul Hutchinson from the Centre of Automotive Safety Research. Prior to his position at CASR he had worked in psychology departments which provided the motivation for this talk. His growing dissatisfaction of descriptions of interactions gave him the stimulus to provide some possible theories for the reason interactions were occurring.

By using 2^2 and 3^2 factorial examples it was demonstrated that there may not only be additive effects occurring but the total of these additive effects have a non-linear relationship with the dependent variable. He proposed that there are four non-linear functions which could describe this non-linear relationship well. These are exponential, logistic, quadratic or cubic functions. In particular a possible theory of a U shaped or inverted-U shaped relationship for his example of terror management theory was discussed. Generally terror management theory hypothesises that a driver's recklessness when they have low mortality salience is no different if

the driver has low or high self-esteem. This type of interaction is generally interpreted as having only additive effects on 'mood' which increases driver's recklessness. However, he went on to show that a U shaped theory to explain the relationship between mood and driver's recklessness proved adequate. This indicated a possible non-linear relationship that had previously been ignored.

He went on to discuss the possible ambiguity in choosing a superior non-linear function to describe a theory. This could only encourage positive debate on the theories of psychology. The meeting finished with some interesting questions which highlighted the possibility of using Generalized Linear Models in a similar way to describe these non-linear relationships.

Janine Jones

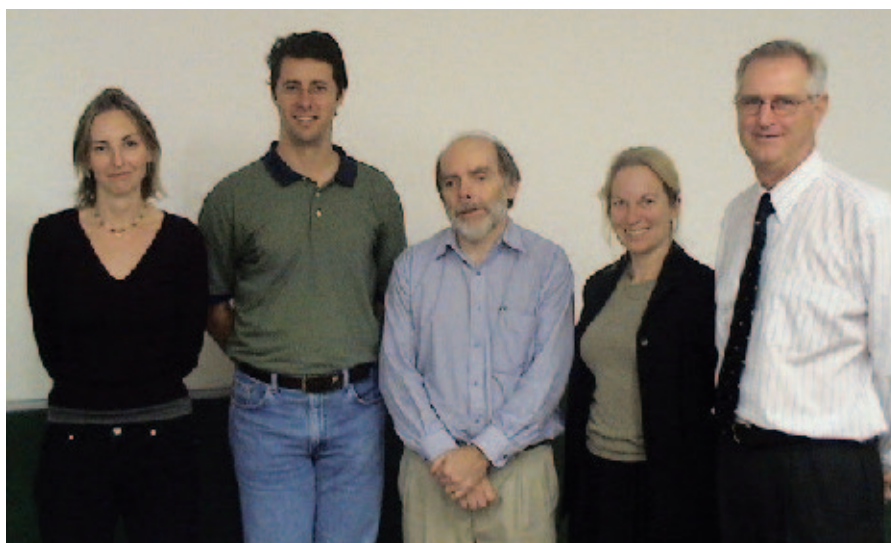
QUEENSLAND

May 2005 Branch meeting

The branch meeting was held on Tuesday, 3rd May, 2005 at the University of Queensland.

Professor John A. Eccleston of University of Queensland, welcomed the speaker Professor Geoff McLachlan from Mathematics at University of Queensland, whose talk was entitled 'A Role for Statistics in Bioinformatics'.

Geoff entertained twenty participants with a lively discussion of the emerging discipline of bioinformatics. Although the definition of bioinformatics is still



Queensland Branch May speaker Professor Geoff McLachlan (center), with SSAI members Helen Johnson (Branch Secretary), Brendan Farthing, Miranda Mortlock (Newsletter Correspondent) and Professor John Eccleston (Branch President).

developing, it is undoubtedly clear that statistics is a major subdiscipline of it. He provided numerical evidence that the explosion of published papers in the area, including some statistics papers, has reached epic proportions and hence increased the burden of keeping abreast of the literature. He went on to outline some problems in bioinformatics in which statistics is playing a major role. These problems reflected his own interest in bioinformatics, which is centred on the statistical analysis of gene expression data. High-throughput assays, such as DNA microarrays, allow the expression levels of tens of thousands of genes to be measured in a single sample. But the high dimensionality of the raw data and the small number of samples pose major problems for statistical analyses. He considered some of these problems and looked at ways in which standard methodology can be modified to handle them. These included supervised clustering, two way clustering, FDR (false discovery rates) and also mixtures of factor analysers. The latter has been implemented in the emmix-gene software.

Geoff McLachlan is professor of statistics in the Department of Mathematics (School of Physical Sciences) at the University of Queensland (UQ) with a joint appointment as a professorial research fellow in the Institute for Molecular Bioscience (UQ). His research interests in statistics include the related fields of classification, machine learning, neural networks, and pattern recognition, and the field of statistical inference. The focus in the latter field has been on the theory and applications of finite mixture models and on estimation via the EM algorithm. More recently, he has been working in the field of bioinformatics. He is the author or co-author of five monographs in these fields.

Awards Evening for the School of Mathematical Sciences at Queensland University of Technology

Other activities in May included a very well attended Awards Evening for the School of Mathematical Sciences at Queensland University of Technology, which was held in the Gardens Theatre Foyer on the 6th May. One of our local SSAI members, Dr Rob Reeves received an award. The function was well attended and the School of Mathematical Sciences had a record number of awards for excellence in mathematics. The Office of Economic and Statistical Research



Harry Bartlett, Ron Webster, and Dr Rob Reeves with his partner Rhonda and daughter Alex at the Awards night for the School of Mathematical Sciences, QUT.

sponsors three three-year scholarships – Robert Russell (Bachelor of Mathematics) was awarded the 2004 scholarship, and Teyl Engstrom (Bachelor of Mathematics/

image analysis, spatial statistics, Bayesian Statistics, stochastic processes.

Dr Friel's talk was entitled 'Bayesian model selection for partially observed diffusion models'.

In this he presented an approach to Bayesian model selection for finitely observed diffusion processes. This problem was tackled using data augmentation by treating the paths between observed points as missing data. For a fixed model formulation, the strong dependence between the missing paths and the volatility of the diffusion was broken down by adopting the recently presented method of Robert and Stramer (Biometrika, 2001). He described how this method may be extended to the case of model selection via reversible jump MCMC. In addition he extended the formulation of a diffusion model to capture a potential non-Markov state dependence in the

drift. Issues of appropriate choices of priors and efficient trans-dimensional proposal distributions for the reversible jump algorithm were also addressed. The approach was illustrated using simulated data and an example from finance.

Several members joined Dr Nial Friel for an enjoyable dinner at South Bank afterwards.

Miranda Mortlock



Kristen Gilshenan (Bachelor of Mathematics/Bachelor of Information Technology) pictured with Professor Tony Pettit having received an award for her second year maths studies.

Bachelor of Business) received the 2005 scholarship.

June Branch Meeting

On 7 June, 2005, we had a Branch meeting at Queensland University of Technology. Our speaker was Dr Nial Friel from Department of Statistics, University of Glasgow. Nial is a lecturer in Statistics and his research interests include MCMC theory and applications,

VICTORIA

At the Branch Annual General Meeting in March, Kay Lipson stepped down as Victorian Branch President. Kay's two year term was marked by a number of innovations, including the most successful Workshop the branch has ever held. She also attracted two well-known International Statisticians to present the 2003 and 2004 Belz Lectures – previous Belz Lecturers had either been born in Australia, or were current residents.

A new Branch Council was elected at the AGM. It consists of Brian Phillips (President), Kay Lipson (Past President), Ann Maharaj (Secretary), Geoff Laslett (Treasurer and SSAI Newsletter Correspondent), Derchie Hung (Webmaster), Kym Butler, Ian Clark and Mervyn Silvapulle. The major issue confronting the Branch is the location of monthly meetings. Some people find the venue (Swinburne University) somewhat inconvenient, although any location would disadvantage a considerable proportion of the membership. The Branch Council discussed the possibility of holding some meetings at other locations.

Victorian Statisticians can now breathe a collective sigh of relief. The Chair of Statistics in the Department of Mathematics and Statistics at the University of Melbourne has been vacant for several years, but has at last been filled by Richard Huggins, formerly of La Trobe University. Richard is taking up his new position in July 2005, returning

early from a two-year appointment as a Professor in the Centre of Mathematics and its Applications at the Australian National University. Richard's publication record is formidable, with substantial contributions covering the spectrum from theoretical to applied. The Branch Council looks forward to cooperating with him in promoting statistics in Victoria.

Mervyn Silvapulle, also formerly of La Trobe, has taken up a Chair in the Department of Econometrics and Business Statistics at Monash University's Caulfield Campus. Mervyn has recently published a monograph entitled *Constrained Statistical Inference* (Wiley, 2005) with P.K. Sen. Mervyn is very active in the Statistical Society. As well as being a Branch Councillor, Mervyn serves as an Associate Editor of the ASNZJS.

The departure of two senior staff members has precipitated the La Trobe University Statistical Science Section into a rebuilding phase. I have invited Paul Kabaila, Head of Statistics at La Trobe, to write more about this in a future issue.

Jeremy Anderson, foundation professor of epidemiology and biostatistics at the University of Melbourne, died of colon cancer in February 2005. A moving tribute to this witty, larger than life character can be found at

<http://bmj.bmjournals.com/cgi/content/full/330/7495/848/DC1>

Following Professor Anderson's premature death, the University of Melbourne has reorganised its epidemiological activities. The Centre for Molecular, Environmental, Genetic and Analytic Epidemiology has been created by merging the Centre for Genetic Epidemiology and the Epidemiology and Biostatistics Unit in the School of Population Health. The new name acknowledges that modern epidemiology combines traditional methods (surveys and questionnaires) with genetic and molecular information. It also bestows upon the world a clever acronym, the Centre for MEGA Epidemiology. (Who said statisticians can't market themselves?!) The inaugural Director is Professor John Hopper.

As reported in the last issue, four Victorian Young Statisticians (Natalie Karavarsamis, Martin Donadio, Tristan Barnett and Derchie Hung) attended the 55th Session of the ISI in Sydney in April after winning Denise Lievesley Awards. They all participated enthusiastically in the conference, learnt a lot, made some good contacts and had a great time.

Geoff Laslett

Discrimination and Molecular Marking in Mass Spectroscopy: A Functional Data-Analytic Approach

At the March meeting Professor Don Poskitt of the Department of Econometrics and Business Statistics at Monash University presented an excellent seminar, based on his joint work with S. Arivalzahan (known as Arivu among his colleagues). The main aim of the project is to ascertain if the statistical characteristics of mass spectra (proteomic spectra or chromatograms) could be readily used to discriminate between individuals in different health states and to develop an appropriate statistical methodology. For example, ovarian cancer is difficult to detect in its early stages of development, and some kind of diagnostic to decide if someone is prone to this disease would be very helpful. In the work reported on, a technique for dimension reduction and density estimation that is based on treating observed chromatograms as realizations of random curves was suggested.

First, note that the observation, namely the proteomic spectrum, from each person is a curve. Thus, each observation is potentially a



Denise (centre) with the Award winners at Darling Harbour, Sydney.

Photo: Brian Phillips



Don Poskitt in his Chair at Monash University

vector having an infinite number of components/variables. This raises several challenges because the number of variables is larger than the number of observations. For the purposes of numerical implementation, the curve is reduced to a vector of its ordinates on a fine grid of points (say 15000) on the mass-charge or 'x'-axis; this may lose some information but hopefully not much because the grid is quite fine. If there are 200 people in the sample, this still leaves us with 200 multivariate observations on 15000 variables. Therefore, to make any progress, there is a need to reduce dimension without losing any important information.

Don and Arivu suggested a way of reducing the dimension of the data using a technique originally developed by Don in conjunction with Peter Hall and Brett Presnel for the analysis of radar signals. The idea is to represent the curve from each subject as a linear combination of a finite collection of data determined basis functions. This technique is sometimes referred to as 'empirical orthogonal functions'. This functional data-analytic view of mass spectra was then used as a basis for patient discrimination and classification using a non-parametric approach to likelihood estimation and evaluation. Don and Arivu also showed how Sensitivity and Specificity, two important indices of the performance of a medical diagnostic test, could be explicitly employed to determine what basis functions should be used to represent the data. This offers an alternative methodology to classical approaches such as proportion of variation explained or thresholding.

The method was illustrated using a set of data relating to ovarian cancer. This data set consists of 216 individuals.

Among them, 100 are ovarian cancer patients, another 100 are controls, and the remaining 16 belong to a benign group. The method appears to work well (questions about the quality of the data raised by the audience and acknowledged by Don and Arivu notwithstanding). This suggests that the methodology may provide a sound basis for the subsequent development of techniques for extracting the molecular characteristics of different individuals and constructing molecular markers. This is work in progress, and I am confident that we will see more developments of the approach in the near future.

Mervyn Silvapulle



Larry Weldon. Photo: Brian Phillips

Simulation as a data-analytic tool for complex systems

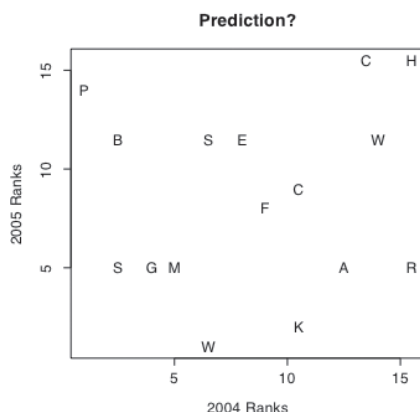
The presentation to the April meeting was given by Larry Weldon. Larry is visiting Brian Phillips' Statistics Unit at Swinburne University for several months while on a study leave from Simon Fraser University in British Columbia. Larry's thinly disguised objective was to encourage use of simulation and graphics in both teaching and practice of statistics. His perspective on the topic was that simulation in combination with a little data can produce more information than either simulation or data alone.

Larry used four examples to make his case: the variability of league standings for equally matched teams with reference to the current footy league, the accordion phenomenon of heavy traffic, the connection between lifetime health status and cross-sectional hospital experience, and an economic optimization problem based on real data for a bakery's deliveries and sales. His back-and-forth between Power Point slides and simulations in the freeware language R kept the audience awake for the full fifty minutes. The discussion continued after the talk and over dinner at a nearby restaurant.

The role of the statistician in the Market and Social Research Industry

At the May meeting Helen Bartley and Mark Davis gave a lively presentation to more than 30 members of the Victorian Branch. Helen and Mark have both worked in the market and social research industry for a number of years in roles where their statistical knowledge has been central to their roles. Helen is an Accredited Statistician and Qualified Practising Market Researcher with a Master of Applied Science in Social Statistics.

After more than 20 years working in government and the private sector Helen established her own business which provides specialist research, statistical



Predicting ALF 2005 ranks from 2004 ranks after 6 rounds



Helen Bartley and Mark Davis. Photo: Brian Phillips

and data management services. Helen also teaches in Swinburne University's graduate program in Applied Statistics. Mark Davis has an honours degree in statistics and a Graduate Diploma in Social Statistics. He has worked in the market and social research industry for more than 15 years. He is currently employed in a senior role at I-View where he is responsible for a range of large scale social research projects.

Helen and Mark began their talk by asking the audience to provide some ideas of their understanding of the

market and social research industry and their perceptions of the role of the statistician in the industry. Notably the audience's understanding of the industry focussed on the annoying calls that many people receive during meal times from telemarketers and interviewers. Helen and Mark then proceeded to explain the role of the industry, emphasising the range of research undertaken by the industry – from traditional consumer research projects through to complex government and social research projects. They commented that the work of the market and social research statistician extends well beyond the traditional areas of data collection and analysis.

Their talk provided some insights into the expectations of a statistician in the market and social research industry. They made the point that an experienced statistician will commonly be involved in all stages of the research process – from preparing a survey proposal, through to monitoring the data collection, undertaking the analysis, reporting and presentation of the results.

They identified the additional skills, beyond the core statistical

training, required to work as a statistician in the industry. In particular they emphasised the importance of being able to communicate effectively, work with others, liaise with clients and have strong verbal and written presentation skills. Other relevant skills include commercial knowledge and experience, an ability to think laterally and a practical mind.

They demonstrated, through examples from their own careers and anecdotal feedback from other market researchers, that the market and social research statistician cannot hide in a back office speaking a language few can understand!

They concluded their talk with examples of job opportunities for statisticians seeking careers in the market and social research industry, and suggested that opportunities were good for statisticians seeking more than a back room position.

Their talk resulted in considerable discussion, specifically about the training required to work as a statistician, how educators should be preparing graduates for a career in the industry and, more generally, about the differences between statisticians working in a commercial environment and those working in an academic environment.

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