



International Society for Clinical Biostatistics

News

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Editorial

Congratulations to the organisers of the Szeged conference for putting together a very well-organised and enjoyable meeting.

"Organise an ISCB Conference? Yes, no problem." That's what Simon Day wrote in ISCB News, #14, June 1993, and reading through the article, I was amazed at how many features of organising the Cambridge conference remain the same in 2005. Having said that, each conference has many unique features. Read more on p.14.

Thanks to the contributors to this News: John Whitehead, Harbajan Chadha-Boreham, Harry Southworth and the many excellent book reviewers, Michael Schemper and Marie Reilly.

Financial News

From the Treasurer & Permanent Office

Because of the high bank charges, which ISCB incurs when you send us local cheques drawn on a non-United Kingdom bank, we are afraid that these cannot be processed. So please make sure that your cheque is drawn on a bank in the United Kingdom or alternatively, pay by credit card or bank transfer. Thank you!

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ISCB Membership

		end 89	end 92	Dec 93	Dec 94	Dec 95	Dec 96	Dec 97	Dec 98	Dec 99	Nov 00	Nov 01	Dec 02	Nov 03	Nov 04	Nov 05
*=host of	conference															
	Total	261	596	715	698	725	702	685	729	818	797	837	825	756	758	620
	# Countries	23	32	32	31	33	34	37	37	41	40	45	41	40	38	39
1.	UK	50	90	176*	120	144	121	128	169*	135	151	153	141	190*	140	109
2.	USA	18	45	40	39	41	40	79*	66	76	77	89	78	75	57	51
3.	Germany	30	67	75	84	71	78	72	70	186*	90	87	77	61	57	51
4.	Poland [NatGrp]		11	11	24	24	30	21	19	26	34	37	41	41	43	40
5.	Hungary [NatGrp]	1	21	17	18	19	25*	27	29	29	33	34	41	48	42	38*
6.	Denmark	4	58*	38	31	30	32	26	35	38	39	36	46	41	37	37
7.	Netherlands	14*	30	38	33	36	29	31	39	35	33	38	39	33	87*	35
8.	France	30	52	62	50	73	67	52	52	49	53	37	93*	31	41	30
9.	Romania [NatGrp]						2			4	1	1	1	19	21	30
10.	Sweden	23	51	53	54	58	64	51	45	38	44	88*	50	36	34	24
11.	Belgium	13	22	27	30	30	32	35	29	25	33	36	33	23	27	24
12.	Switzerland	14	25	22	80*	33	29	24	25	23	18	23	26	22	23	23
13.	Japan	2	6	7	5	7	4	10	13	20	12	11	10	10	10	17
14.	Italy	16	33	37	32	32	33	26	33	26	63*	29	25	15	25	15
15.	Austria	4	9	11	13	11	16	13	11	15	18	15	13	16	17	15
16.	Norway	13	18	25	22	12	18	10	10	11	10	16	16	12	14	12
17.	Canada	6	12	14	14	11	13	15	14	9	9	10	14	16	8	12
18.	Finland	2	7	7	9	9	9	7	5	10	9	18	11	7	11	10
19.	Australia	6	9	11	6	9	8	11	9	10	12	8	9	14	8	6
20.	Spain	10	12	18	12	46*	23	14	16	12	11	11	8	7	15	5
21.	Singapore							3	6	4	5	8	5	7	2	4
22.	Israel	1	3	4	4	4	4	3	3	4	10	13	10	7	8	3
23.	Slovenia		1	2	3	2	1	1	3	2	1	2	1	2	3	3
24.	Malaysia					2	1	2	2	1	1	1	1	1	3	3
25.	South Africa		1	4	1	3	2	2	2	2	2	3	3	3	2	3
26.	Czech. Rep.			1	1	1	1	1	1	2	2	1	1	1	1	3
27.	India		1	1	1	1	1	1	1	1	2	1	2	2	3	2
28.	Greece		1	1	1				1	1	3	1	6	1	2	2
29.	Turkey		1	1						1				1	2	2
30.	New Zealand		1		1		2	1	2	2	2	3	3	3	1	2
31.	Iran						1	1					1	1	4	1
32.	Russia					1	3	3	3	2	2	1	4	3	2	1
33.	Mexico						1	1	1	1	1	1	2	2	2	1
34.	Cuba								2	2	2	2	2		2	1
35.	Portugal	1	3	5	2	2	2	2	5	5	3	4	3	3	1	1
36.	Taiwan										1	1	1	1	1	1
37.	Estonia											2		1		1
38.	Slovakia												1			1
39.	United Arab Emirates															1
40.	Malawi												1	1	1	
41.	Ireland	1	2	3	4	3	4	4	2	3	2	3		1	1	
42.	South Korea					3		1						1		
43.	Colombia							1	1		1			1		
44.	China		1	1	2	3	3	3	3	3	3	3	2			
45.	Thailand		1	1		1	1	2	1	1	2	2	2			
46.	Croatia									1	1		1			
47.	Gambia												1			
48.	Lithuania											2				
49.	Argentina											1				
50.	Brazil					2						1				
51.	Kuwait	1										1				
52.	Saudi Arabia											1				
53.	Sudan											1				
54.	Ukraine									1		1				
55.	Egypt											1				
56.	Pakistan								1	1	1					
57.	Philippines									1						
58.	Indonesia						1									
59.	Zimbabwe				1											
60.	Kenya		1	1												
61.	Oman	1														

President's Year End Message

From John Whitehead

The turn of the year is a good time to reflect on the Society's achievements during 2005 and to look forward to the activities of 2006. Our Annual Scientific Meeting in Szeged in August was a great success. Scientifically, a full range of ISCB interests were covered. New topics such as the effects of genomics on clinical research were well represented, but old battles such as whether to analyse change from baseline or to adjust through analysis of covariance were returned to. While extending the frontiers of our expertise, statisticians in particular appear to have to constantly guard the territory won years ago from incursions by "experts" from other disciplines. Szeged also turned out to be a perfect location for ISCB's relaxed and friendly style of meeting. Participants discovered an attractive and historic city, a modern and well equipped conference centre and a most enjoyable social programme. The number of participants was a little lower than we had hoped for, but many new members were sufficiently impressed to promise to attend our meeting again, which is a valuable contribution to the future of the Society. I should like to thank again both the Scientific Programme Committee and its Chair, Michael Schemper and the Local Organising Committee and its Chair, Julia Singer for their work in making the conference such a success.

Three of our Subcommittees are now under new Chairs. Michael Schemper founded the National Groups Subcommittee, and put enormous effort and energy into setting up our Groups in Hungary, Poland and Romania. The founding of a fourth group in the Czech Republic is the subject of a Society-wide electronic ballot at the moment. Michael also instituted the Conference Awards for Scientists to encourage participation by statisticians from the countries of Eastern Europe and the Third World. Both schemes have been very successful, the meeting in Szeged being just one fruit of this activity. Michael is now standing down from Chairing the

National Groups Subcommittee, and over the coming months will be handing over to Julia Singer, who as an energetic member of the Subcommittee and leading player within the Hungarian National Group is in many ways his natural successor. Marie Reilly is handing over the Chair of the Student Conference Awards Subcommittee to Kyungmann Kim. Marie has capably directed this valuable and successful programme for four years, introducing new and promising statisticians to our Society, and I am sure that Kyungmann will carry on the good work. Finally, Carol Redmond is stepping down from the Education Subcommittee. Carol has organised the presentation of courses in various "ISCB target countries", and these have been much appreciated. She hands over to Rumana Omar who, rather bravely as a newcomer to the Executive Committee, has agreed to take this on. I would like to thank Michael, Marie and Carol for their valuable service to the Society, and Julia, Kyungmann and Rumana for stepping into their shoes.

A new Subcommittee, approved at the last AGM, is that for Membership. Emmanuel Lesaffre is currently putting together his team for tackling the challenge of maintaining and expanding the Society's membership. A major factor in keeping our membership numbers healthy is attracting people to our conferences. In this respect, the Geneva meeting in 2006 is shaping up very well. The scientific programme is exciting, and the location is easily accessible, attractive, and not as expensive as some might fear. Lutz Edler and David Warne are doing excellent work as Scientific Programme Chair and Local Organising Chair respectively. It will be an excellent meeting, and so I call on members to support the Society and join us in Geneva, and to pass the word around colleagues, especially young colleagues who may not yet know about our work, and encourage them to come too.

A Happy New Year to you all!

Book Review by Tiberiu Postelnicu (Romania)

Harvey Motulsky and Arthur Christopoulos	Fitting models to biological data using linear and nonlinear regression: A practical guide to curve fitting	Oxford (2004) 0-19-517180-2
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Most biologists use nonlinear regression more than any other statistical technique, but there are very few places to learn about curve fitting. This book clearly and succinctly addresses this focused need of an extraordinarily broad range of scientists. Written for biologists, it presents a practical approach to fitting curves. The authors explain how to choose a model, how to make sensible choices when using a nonlinear regression program, and how to interpret the results. In addition to general information about curve fitting, this book discusses specific details about fitting radioligand binding, dose-response, and enzyme kinetic data, emphasizing the use of global regression.

The book is written as a companion to the software package GraphPadPrism (version 4) and contains 10 Sections denoted with capital letters. The first Section, *Fitting data with nonlinear regression* begins with an example of curve fitting, followed immediately by a discussion of how to prepare the data for nonlinear regression, the choices need to make to run a nonlinear regression program, and how to interpret the results and troubleshoot problems. Once we have completed this first Section, we are ready to analyse the own data and can refer to the rest of this book as needed.

The next Section is *Fitting data with linear regression*, and explains this type of regression separately because linear regression is usually performed separately from nonlinear. Section C deals with *Models*, because linear and nonlinear regression fit mathematical models to the data to determine the best-fit values of the parameters of the model. Examples of simple models, tips on choosing a model, global models and compartmental models are given. Next, *How nonlinear regression works* is presented: modeling experimental error, unequal weighting of data points, how nonlinear regression minimizes the sum-of-squares. In the Section *Confidence intervals of the parameters* we find: Asymptotic standard errors and confidence intervals, Generating confidence intervals by Monte Carlo simulations and via model comparison,

Comparing the three methods for creating confidence intervals, Using simulations to understand confidence intervals and plan experiments.

When fitting biological data with regression, the main objective is often to discriminate between different models. Therefore the aim of the next Section is *Comparing models*, with the following topics: Comparing models using the extra sum-of-squares *F*-test, Comparing models using Akaike's Information Criterion, Examples of comparing the fit of two models, Testing whether a parameter differs from a hypothetical value. Section G gives an answer for the question *How does a treatment change the curve?*, namely: Using global fitting to test a treatment effect in one experiment, Using two-way ANOVA to compare curves, Using a paired *t*-test to test for a treatment effect in a series of matched experiments, Using global fitting and unpaired *t*-test. Analyses in *Fitting radioligand and enzyme kinetics data* are based on a simple molecular model called the law of mass action and the following aspects are presented: Analyzing radioligand binding data, Calculation with radioactivity, Analyzing saturation, competitive and kinetic binding data, Analyzing enzyme kinetic data. The aim of the next Section is to present the problems of *Fitting dose-response curves*: The operational model of agonist action, Dose-response curves in the presence of antagonists, Complex dose-response curves. The last Section has the objective *Fitting curves with GraphPadPrism*. Prism combines scientific graphics, basic biostatistics and nonlinear regression and is available for both Windows and Macintosh.

This well-written book fills a major need for biomedical researchers and the authors do an excellent job explaining the principles of curve fitting along with practical discussions of how to pick a model, how to make sense of results, what to do when the results appear to be nonsense and, how to compare curves. It is a very useful book for all doing research in pharmacology, biophysics, or biochemistry.

This book, originally published in 1997, has been released as a hardback by Chapman & Hall/CRC in 2002 at the price of \$94.95. Amazon gives the price of \$79.61 or £53.99. The book consists of 10 chapters (265 pages). The authors have a long-standing experience in this topic with the Southwest Oncology Group (SWOG) and aim to provide a non-technical review of methods and issues related to clinical trials in oncology. As the authors point out, the book could be of use in clinical trials more generally as it discusses issues and concepts that are important in any clinical setting.

Chapter 1 provides a brief history of clinical trials, introduces the Southwest Oncology Group, describes the trials that are used as examples throughout the book and states the aims of the book.

Chapter 2 introduces basic statistical concepts such as different types of outcome measures (qualitative, quantitative), probability of an outcome, distribution and probability density function. Then, the authors introduce some further statistical concepts related to the different types of clinical trials (phase II or III) and outcomes (response, survival). For phase II studies, the concepts of estimate and confidence interval are provided and the dependence of the width of the confidence interval on the sample size is discussed. It should be noted that no formulas are provided in this section. For phase III studies, a very brief comment on the necessity of randomisation is provided and then issues relevant to hypothesis testing (one/two-sided, X^2 test, type I/II error, power, p-value) and survival analysis (censoring, Kaplan-Meier estimates, log-rank test, proportional hazards model) are discussed. Sample size calculation for a clinical trial is briefly discussed and a formula is provided for the case of dichotomous outcome.

Chapter 3 deals with the design of clinical trials. Some basic elements that have to be considered in the design of a trial - such as primary objectives, eligibility criteria, assumptions for sample size calculation, definition of various endpoints - are presented. Then, the design of phase I, II and III studies is discussed. The traditional design for phase I studies (Fibonacci design) is introduced and the reasons for not being optimal are presented. Then, the authors review briefly various improvements in phase I designs such as designs that are more flexible with respect to re-escalation (up and down designs), continual reassessment methods and pharmacokinetically guided dose escalation (references from 1990-2001). Phase II trials are then introduced and the standard SWOG phase II design is discussed. Randomised phase II designs are introduced for the special case where the aim of the trial is to decide which of

several new regimens should be taken to the next phase of testing. Other phase II designs are briefly reviewed (designs that minimize the expected number of patients, pilot studies, designs that formally incorporate response and toxicity into the decision rule etc). The discussion of phase III trials design includes a more detailed review of randomisation (stratification factors, randomisation schemes, blinding, timing of randomisation) and of hypothesis testing in two-arm trials. This chapter concludes with a brief review of equivalence and non-inferiority trials.

Chapter 4 deals with multi-arm trials. The authors note that this type of trials should be avoided. They discuss various types of multi-arm trials (all comparisons of interest, one control vs. multiple experimental drugs, factorial design etc). Then, the issues of multiple testing, power and interaction are discussed.

Chapter 5 concentrates on interim analysis and on data monitoring committees. The authors present the caveats of interim analyses, stress that these have to be planned and, then, discuss the standard approach used by SWOG on this issue. Subsequently, they provide a very detailed description of the responsibilities and the composition of data monitoring committees. The chapter concludes with several examples of trials that were early terminated due to the review of the results of interim analyses by data monitoring committees.

Chapter 6 deals with data management and quality control. The authors present examples of what can happen if data quality is bad. They provide a detailed description of what a study protocol should contain. Then, they discuss the issue of data collection (which categories of variables should be included, basic data items that have to be collected in all studies) and data forms (an appendix with sample data forms is also provided). A very detailed account on data flow and evaluation of data is presented. The chapter concludes with some comments on the necessity of quality assurance audits and on database management.

Issues on the reporting of results are reviewed in Chapter 7. More specifically, the authors discuss the timing of reports in phase II and phase III trials and the information that has to be included. Various issues relevant to the analysis of the data (intention-to-treat approach, summary statistics that have to be reported depending on whether the outcome of the study is response, survival or quality of life) as well as the interpretation of results (e.g. non-significant tests in studies with low power) are also discussed. The authors conclude by pointing out that patients' lives may depend on what is reported.

Chapter 8 discusses the various problems that are encountered with analyses used to draw conclusions beyond those supported by the study

design. The problems that are encountered with the use of historical controls are reviewed with the help of real examples. The concept of competing risks is also presented and the appropriate methods of analysis are briefly reviewed (cumulative incidence curve, cause specific hazards). The pitfalls of outcome-by-outcome analysis, subset analyses and of using surrogate endpoints are also discussed.

Chapter 9 deals with exploratory analysis serving to generate and not to prove hypotheses such as identification of prognostic factors, forming prognostic groups, analysis of micro array data and meta-analysis.

Chapter 10 summarises the main points and the conclusions of the book.

The book is well written and provides a review of issues related to clinical trial in a non-technical way. The latter may be appealing to clinicians although I think that some readers may be annoyed by the fact that formulas are kept to the minimum in this book. What is apparent throughout this book is the commitment of the authors towards the patients participating in the trials. The feeling you get while reading about statistical significance, power and reporting of results is that these issues are not just theoretical considerations but they are directly related to the patients' lives and well-being. I found this aspect of the book very appealing. Another strong point of the book is that the authors illustrate the various concepts and pitfalls in the design and analysis of clinical trials through the use of real examples from SWOG trials. Furthermore, the book contains numerous up-to-date references; approximately one third of the references were published from 1995 and onwards.

It should be pointed out that since the authors aimed at reviewing a wide range of methods and concepts in clinical trials, this is done sometimes quite briefly. Even common issues such as sample size calculation and randomisation are not described in a way that someone could actually be able to apply them after having read the relevant chapters. For example, a formula for sample size calculation is provided only in the case of dichotomous measurements and no tables of random numbers or for random permuted blocks are provided. Other types of clinical trials such as crossover trials or sequential trials are not discussed.

To summarise, I would highly recommend this book to clinicians who are involved in clinical trials. Statisticians or students who want to go deep into important concepts and issues in the design and analysis of clinical trials would benefit by using this book as a supplementary text.

From Lutz Edler

Dear Members of ISCB,

When it becomes colder in Europe and the Christmas Markets have started to attract people in Central Europe and elsewhere, i.e. when one year is coming to an end and the next is approaching, it is tradition in ISCB to invite you to the next annual meeting of our Society.

So with this Newsletter, you will find the invitation brochure for the 27th Annual Conference of the International Society for Clinical Biostatistics. The brochure gives you all the details of the conference, from the overview and the lists of people behind the scenes and those who are already on stage to the valuable information about the site which is Geneva, one of the most international cities of the world, located in the French-Swiss southwest corner of Switzerland where the river Rhone flows out of the Lac Lemman*.

The scientific programme which you will find in the enclosed brochure has been built up in a joint effort of the Scientific and the Local Programme Committee with a remarkable support from a number of members of the ISCB Executive Committee and – last but not least - with the help of the speakers and discussants themselves who were contacted by the members of the SPC and asked to contribute to our conference.

As you will easily notice from the brochure, ISCB 27 or ISCB 2006 (whatever you prefer) is based on 4 pillars

- the 5 Invited Sessions, including the ISCB President's Invited Session scheduled, in ISCB tradition, for Wednesday before the General Assembly,
- the 5 Special Sessions, which have been designed to cover topics of special interest groups within ISCB and can be thought of (but are not really) a replacement for the mini-symposium for this conference,
- the block of the Contributed Sessions for which we advertise a number of preferred topics besides all those additional themes and topics submitted by you until 15 March 2006, the deadline for submission of abstracts (PLEASE COMPLY WITH THIS DATE!), and
- the 4 Pre-Conference courses with which the Conference will start on Sunday 27 August 2006.

The programme has already grown so large, that it is hard to describe it without missing important parts in a letter such as this. Therefore, please study the details on the 8 pages of the brochure. There you will find the classical span of ISCB ranging from the design of clinical trials to statistical modelling and statistical data analysis. As a highlight, ISCB President John Whitehead has chosen the topic of Adaptive Designs and invited the most outstanding protagonist of this field, Peter Bauer from Vienna University, for this distinguished ISCB lecture (a series which started in Heidelberg in 1999!).

Adaptive Designs will be a major topic of ISCB 2006 since it is also a topic of a regular invited session. With Drug Sensitivity and Drug Resistance, we have included a new field and we have taken up the older field of Competing Risks for which new results will be presented and discussed. Another highlight is in Regulatory Affairs, which is expected to become

provocative and very relevant for all colleagues working in pharmaceutical companies, which means we are looking North towards Basel, just to mention one place.

As mentioned above, the Special Sessions will take the place of the traditional mini-symposium and if you long for it and if you miss it in Geneva, allow us to answer: We have 5! We offer 5 deliberately very different topics ranging from statistical methodology such as Robust Methods and Variable Selection to 2 fields of applications which are usually not so in the focus of biometric or biostatistical conferences, namely Subfertility and Dentistry Studies. Last but not least, and also giving reference to Geneva as a Human Health City, with the help of Lara Wolfson from WHO and LOC, we have established a session on WHO Statistics, with the obvious aim to seek communication with this agency and to awake the interest of ISCB members to the important and valuable work of this sub agency of the United Nations, an aim which fits to ISCB's first letter, i.e. of being International.

We identified four themes for the traditional pre-conference courses with distinguished lecturers all well known for their special knowledge in the respective field and we encourage you to take up this offer of continuing education in ISCB. We are sure that receiving training from those experts will be of a real benefit in the work coming up on your desk.

We have also identified a number of topics called Preferred Contributed Topics which might be of interest to smaller or larger subgroups of scientists within and outside of ISCB and we intend to build on these themed special Contributed Sessions during ISCB 27. By no means this should be interpreted as a restriction of the ISCB 2006. Those topics should be considered simply as kernels and we invite you all to define more of those.

During ISCB 27, the ISCB will again offer Student Conference Awards (contact Marie Reilly) for post graduate students who have to register and Conference Awards for Scientists (contact Michael Schemper) to enable scientists from the so-called ISCB target countries to attend the conference. Please apply, therefore, if you are entitled, or encourage colleagues you know who could benefit from such an award to apply before 15 March 2006.

It was obviously the bridge over the river Rhone which drew Caesar's attention to "Genava" on his way to Gallia. Meanwhile the city and canton of Geneva has more than just one bridge and the river is has become a minor land mark compared with the city and its famous buildings and, in particular, compared with the lake and its fountain, "Jet d'Eau". But you will cross the bridges many times when attending ISCB 2007 and we hope that you can build bridges with your friendly colleagues as they always gather at ISCB's Annual Conference.

*described in C. Julii Caesaris Comentariorum de Bello Gallico (53 B.C.) as follows: Rhodanus fluit isque non nullis locis vado transitur. Extremum oppidum Allobrogum est proximumque Helvetiorum finibus Geneva. Ex eo oppido pons ad Helvetios pertinet.

MPS Medical and Pharmaceutical Statistics Research Unit

PROFESSIONAL DEVELOPMENT COURSES 2006
AT THE UNIVERSITY OF READING, UK
FOR MEDICAL STATISTICIANS

Week 1

6-8 MARCH

Statistical Methods for Ordered Categorical Data

Presenters:

Kim Bolland, John Whitehead

9-10 MARCH

Sample Size Determination in Clinical Trials

Presenters:

Anne Whitehead, Mark Simmonds

Week 2

19-20 JUNE

Dose-escalation Procedures in
Phase I Clinical Trials

Presenters:

Yinghui Zhou, John Whitehead

21 JUNE

Proof-of-concept Studies

NEW

Presenters:

John Whitehead, Elsa Valdés-
Márquez

22-23 JUNE

Meta-analysis of Clinical Trials

Presenters:

Anne Whitehead, Mark
Simmonds

Week 3

30-31 OCTOBER

Analysis of Multiple Failure Time
Data Arising from Clinical Trials

Presenters:

Patrick Kelly, Anne Whitehead

1-2 NOVEMBER

Adaptive Designs

NEW

Presenters:

John Whitehead, Kim Bolland,
Sue Todd

3 NOVEMBER

Phase II/III Clinical Trials

NEW

Presenters:

Sue Todd, Patrick Kelly

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From Harbajan Chadha-Boreham

The meeting started at 12:00 (before the lunch break) and the agenda was:

- 1 President's report
- 2 Treasurer's report
- 3 Subcommittee reports & motions for continuation:
 - Subcommittee on ISCB Membership – Proposal,
 - Subcommittee on Statistics in Regulatory Affairs,
 - Subcommittee on National Groups,
 - Subcommittee on Education,
 - Subcommittee on Communications,
 - Subcommittee on Student Conference Awards,
 - Subcommittee on Statistics in Dentistry,
 - Subcommittee on Conference Organising
- 4 Future ISCB meetings
- 5 Any other business

1. President's Report (JW)

I should like to thank Julia Singer, the Local Organising Committee and the Scientific Programme Committee for doing a such an excellent job of organising the Society's 26th Annual Meeting in this wonderful and historical city of Szeged. This year, besides having a new President, the Society also has a new Vice-President, a new Secretary, and the majority of the members of our Executive Committee are also new to their roles. Thankfully, the Treasurer remains constant! The Society's business during the year is now organised by quarterly teleconferences between the Officers, and so far we have been discussing the Society's finances, arrangements with *Statistics in Medicine*, preparation for this and future conferences, support in target countries, and the need to increase the Society's membership. The ISCB's Permanent Office is now back in Denmark and we are grateful to Rita Schou and Bjarne Nielsen for resuming the smooth running of our affairs. In this AGM you will hear about the activities of the Society throughout the year. Although the main activity of the ISCB is this, our annual scientific meeting, you will see that we are indeed active throughout the year.

2. Treasurer's Report 2005 (NV)

The financial report for 2004 is attached; it was audited in June 2005 (and fully approved) by Ernst & Young, Statsautoriseret Revisionsaktieselskab (see Attachment 2).

Financial Situation: At the end of 2004, the society's capital stood at € 88,199.43, compared with € 80,970.11 at the end of 2003. This increase of more than € 7,000 (almost 9%) clearly shows that the financial situation of ISCB has been stabilised. We have not yet reached our objective: an equity balancing the costs for an annual conference (Leiden: definitely € 147,235; Szeged: approx. € 150,150; Geneva: approx. € 153,732), but we are on a good way.

Main reason for this good financial result is the surplus from the Leiden conference of about € 20,000. We should be very grateful to the organizers of the Leiden congress to have conducted an event, which was a success scientifically as well as financially! The congress finances were handled in a very efficient way by the congress treasurer, Siem Heisterkamp, and the congress accounts were audited by Paul Mulder, who gave full approval of the Leiden congress accounts.

Regarding the income from membership fees, there was also a small increase, but this does not result from an increase of membership, but from the higher annual membership fees we ascertained for the first time in 2004.

Regarding the positions of expenditure, there were some reductions and increases only in the positions "Officers and ExCom" and "Awards". These cost increases are, however, artificial and not real, because in the London conference (our joint conference with SCT), some positions like "Waiving of congress fees" and "Accommodation for prize winners" were (partly) included in the conference financial statement and not explicitly brought forward in the ISCB expenditures.

Hence, our economy measures were successful, but should be maintained in the future until we will have returned to a total equity of 150,000 €.

To summarize: it must be stated that the income from membership fees is not enough to empower the current expenditure of the society, and that the enjoyable balance of 2004 was only possible by the conference surplus of Leiden. Therefore, our conclusion for the future must be to plan conferences budgets, so that costs connected to the conference (awards, waived fees) are covered by the conference income. The subcommittee on conference organisation has worked hard on the rules for congress organization, and I am sure that these rules will help improving the efficacy of our congress organizing and in reducing the costs.

Membership: As in recent years, the membership development shows a small decrease (attachment 3); especially remarkable is the decrease of paying members (323 members at 30 June 2005 compared to 356 at 30 June 2004). Also, we have to expect a lower number of "members by congress participation" in Szeged, as the total participation in Szeged seems to remain lower than in Leiden. Hence, we have to expect at the end of 2005 a lower membership than at the end of 2004. To enhance the perspectives of ISCB, we need to reverse this trend in starting activities for an enlargement of membership. This problem was the main topic of the 2005 ExCom meeting.

The currency change from British Pound to Euro was carried out, and all figures in the report are now indicated in Euro.

The financial report by 30 June 2005, shows the same tendency as in 2004 and the organiser of the Szeged congress do not expect a deficit.

I do not see any reason to change the membership fees and propose to maintain the fees at € 40.

Heidelberg, 7 July 2005

Norbert Victor

Attachments:

- 1) Financial Report 2004
- 2) Auditors' Report
- 3) Updated Membership Diagram

Norbert Victor remarked during the AGM that:

- the ISCB's finances are back in balance,
- the economy measures are maintained,
- there is a slow decrease in membership and we must have activities to increase membership

The Treasurer's report was approved unanimously by the ISCB participants at the AGM.

ISCB26 Szeged 2005: AGM Report (continued)

Attachment 1: ISCB FINANCIAL REPORT on 31 DECEMBER 2004

	2004 €	2003 €
Income		
Membership fees	22,700.00	18,589.73
Conference surplus	20,084.36	1,129.04
Course surplus		
Advertising	2,800.00	2,512.13
Earned interest	3,074.04	3,248.49
Currency gains	317.43	3,014.85
Total income	48,975.83	28,494.24
Expenditure		
Permanent Office:		
Consumables	22.25	1,266.89
Postage & freight	174.31	346.86
Telecommunication & internet	882.28	1,025.62
Printing & photocopying	75.73	135.35
Travel		76.68
Credit card transaction fee, RfA		894.66
Administration RfA		9,215.45
Administration Medicon	11,194.02	1,886.68
	12,348.59	14,848.19
Officers & ExCom:		
Conference fees	5,200.00	776.84
Accommodation	1,204.16	2,357.09
Travel expenses	685.10	831.47
Other expenses		
	7,089.26	3,965.40
Awards (Students, Scientists):		
Conference fees	3,300.00	
Accommodation	4,115.98	3,363.38
Travel expenses	742.61	
Other expenses	1,254.45	96.90
	9,413.04	3,460.28
Workshops / Courses:		
Honorarium	1,739.52	
Travel expenses	1,166.19	
	2,905.71	0.00
Newsletter:		
Office expenses	6,209.81	9,906.46
Editorial expense		
	6,209.81	9,906.46
Other items:		
Bank charges	1,646.38	319.90
Interest paid		1.08
Audit	1,680.00	2,074.30
Currency loss	453.72	
Loss for unrealisable assets		540.11
	3,780.10	2,935.39
Total expenditure	41,746.51	35,115.72
NET INCOME:	7,229.32	-6,621.48

Continued...

ISCB26 Szeged 2005: AGM Report (continued)

	2004 €	2003 €
Assets		
Bank accounts:		
Barclays GBP current account		1,858.15
Barclays GBP high interest account	12,667.43	10,607.67
Barclays Euro account	10,347.16	3,808.16
Nordea DKK account	5,299.35	6,398.90
Nordea Euro account	33,301.05	
Bonds, Danish State 7% 2004		44,596.82
Bonds, Danish Shipbuilding Fund 2006	44,226.62	
	105,841.61	67,269.70
Others:		
Accounts receivable	854.85	918.72
Leiden conference 2004, surplus	6,615.56	12,103.51
Szeged conference 2005, seed money	4,000.00	
Resources for Associations		1,428.32
London conference 2003		8,542.66
	11,470.41	22,993.21
Total Assets	117,312.02	90,262.91
Liabilities		
Owing to Permanent Office	26,698.59	5,175.03
Audit	1,680.00	3,366.25
Accounts payable		471.52
Prepayment account, members	734.00	280.00
Total Liabilities	29,112.59	9,292.80
Assets less Liabilities	88,199.43	80,970.11
EQUITY brought forward	80,970.11	76,669.10
Equity adjustments by 31 December 2003		10,922.48
Profit by 31 December	7,229.32	-6,621.47
EQUITY carried forward	88,199.43	80,970.11

Conversion rates:

31-12-2003 DKK/EUR 744.46 GBP/EUR 1.4355

31-12-2004 DKK/EUR 743.81 GBP/EUR 1.4373

Attachment 2

AUDITOR'S REPORT

To the members of ISCB: We have audited the Annual Report of ISCB for the financial year ended 31 December 2004. The Annual Report is the responsibility of the Society's Executive Officers and Executive Committee. Our responsibility is to express an opinion on the Annual Report based on our audit.

Basis of Opinion

We conducted our audit in accordance with Danish Auditing Standards. Those standards require that we plan and perform the audit to obtain reasonable assurance that the Annual Report is free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the Annual Report. An audit also includes assessing the accounting policies used and significant estimates made by the Supervisory and Executive Boards, as well as evaluating the overall Annual Report presentation. We believe that our audit provides a reasonable basis for our opinion. Our audit has not resulted in any qualification.

Opinion

In our opinion, the Annual Report gives a true and fair view of the Society's financial position at 31 December 2004 and of the results of its operations for the financial year then ended in accordance with the Constitution of ISCB.

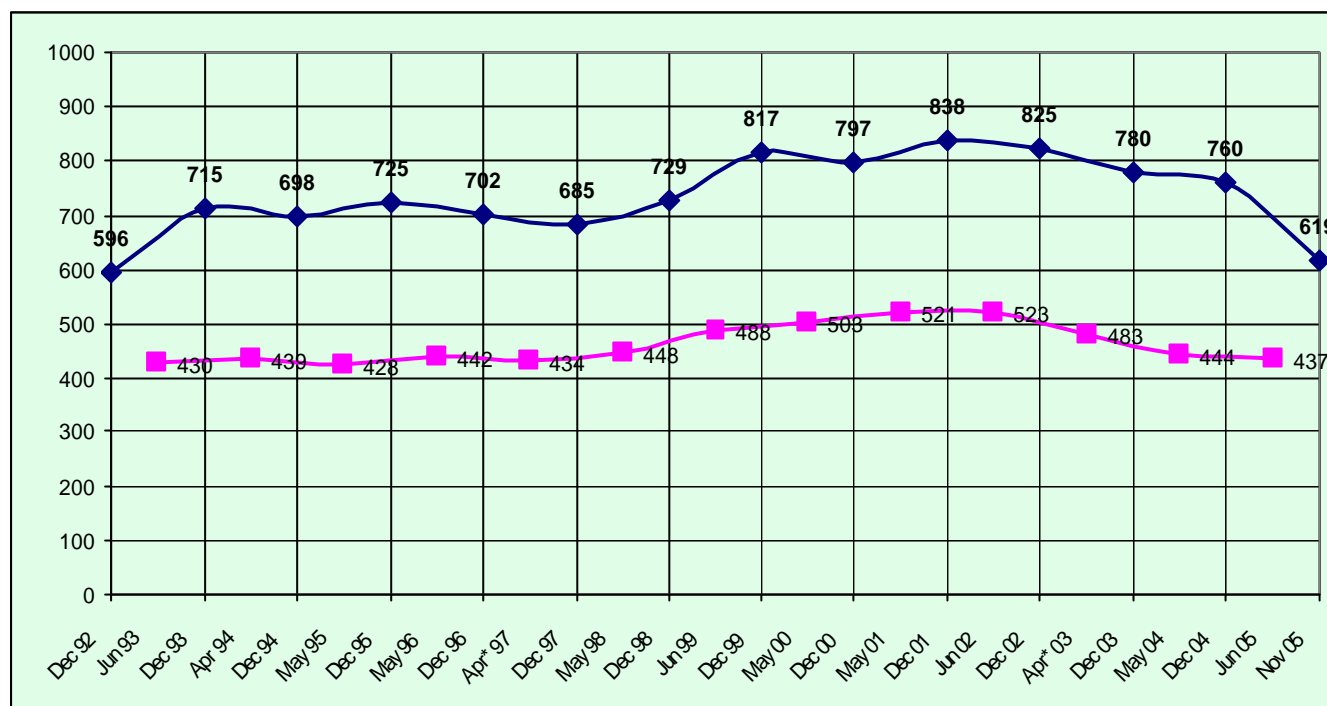
Elsinore, Ernst & Young

Statsautoriseret Revisionsaktieselskab

Marius Jensen

State Authorised Public Accountant

Attachment 3: Progression of Membership 1992-2005



3. Subcommittee Reports

The eight Subcommittee Chairs reported on the activity of their Subcommittee, and the complete reports of seven of them are published together with these minutes in the Newsletter, with terms of reference and list of members. No written report was received from the Education Subcommittee as the Chair resigned. The reports of Subcommittees to the AGM (edited by the Secretary) were:

3.1 Emmanuel Lesaffre on Proposal for ISCB Membership SC

Emmanuel Lesaffre overviewed the Terms of Reference of the newly formed SC and invited the ISCB participants to join the SC. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.2 Jorgen Seldrup on Statistics in Regulatory Affairs SC

Harbajan Chadha-Boreham presented the written SC report of Jorgen Seldrup. There were no offers during the year from the ISCB members to lead the disease or drug specific guidelines. SIRA submitted comments to the EMEA on "Guideline on Data Monitoring Committees". Karsten Schmidt resigned after several years of active service to SIRA SC. HCB invited ISCB members to join SIRA; if interested they should contact Jorgen Seldrup. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.3 Michael Schemper on National Groups SC.

The primary aim of the National Groups SC is to support target countries. A proposal has been received from Czech Republic to join the National Groups SC as a target country. A total of 12 applications for the Conference Awards for Scientists for the Szeged ISCB meeting were received. The National Groups Subcommittee voted to selected the following 8 winning entries: Urszula Biela (Poland), Cornelia Enachescu (Romania), Maria Fazekas (Hungary), Anneke Grobler (South Africa), Piotr Jurkowski (Poland), Stanislav

Katina (Slovakia), Norbert Solymosi (Hungary), Corina Vernic (Romania). The winners received awards from Michael Schemper during the AGM. There will be 6 awards in the future and the rules for funding will be put on the website. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.4 Rumana Omar on Education SC

Carol Redmond resigned as Chair of the Education SC. A meeting of the SC was held in Szeged where Rumana Omar (UK) was elected to Chair the SC and a new member joined, Catherine Quantin (F). The SC proposed that they would aim to put on courses to teach a) statistics to non-statisticians and b) how to referee journals. John Whitehead commented that these courses could be suitable for pre-conference workshops. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.5 David Warne on Communications SC

David Warne stated that it was a normal year for the SC, which is running smoothly. Good work was done by Harry Southworth on coordinating the review of books and if members are interested in reviewing, they should contact Harry. ISCB members enjoy receiving the Newsletter. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.6 Marie Reilly on Student Conference Awards

There were 11 entries received this year and covered a wide geographical areas. The SC selected three winners: Holly Janes (USA), Katherine Lee (UK). Spyridoula Tsonaka (Belgium). Marie Reilly thanked the Szeged Local Organising Committee for helping to make things easier for the SC. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.7 Emmanuel Lesaffre on Statistics in Dentistry SC

Emmanuel Lesaffre reported that the SC is examining the usefulness of the extension of the CONSORT guidelines to clustered data on split-mouth studies. The findings will be reported back to the CONSORT group on the SC's experience with the guidelines. Further, the SC's findings will be reported in a manuscript that we envisage submitting to a peer-reviewed journal. The manuscript will be circulated to the ISCB members for review before submitting it to a journal. There will be a special session on Dentistry at the ISCB meeting in Geneva. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

3.8 Harbajan Chadha-Boreham on Conference Organising SC

The Conference Organising Guidelines were revised during the year with substantial input from David Warne and John Whitehead. Maria Grazia Valsecchi retired from the SC. David Warne and Giota Touloumi joined the SC during the Szeged meeting. The Conference Organising Guidelines will be put on the ISCB Homepage for future conference organisers. The motion for continuation of the Subcommittee was approved by the ISCB participants at the AGM.

4. Future ISCB Meetings

4.1 ISCB27 (2006) in Geneva (Switzerland) by David Warne

David Warne showed views of Geneva and reported on the plans of the ISCB meeting. He assured the participants that Geneva is not really expensive, because a lot of accommodation will be available cheaply and the tours will also be cheap to encourage participation.

4.2 ISCB28 (2007) in Alexandroupolis (Greece) by Giota Touloumi

Giota Touloumi presented the initial plans of the ISCB meeting. The venue in Alexandroupolis is not yet fixed but is likely to be a hotel with a conference centre. A more detailed plan for the meeting is to be submitted to

the ExCom in autumn 2005 and will contain a list of a wider Local Organising Committee.

4.3 ISCB29 (2008) in Copenhagen (Denmark) by Bjarne Nielsen

Bjarne Nielsen gave a preliminary presentation of the plans for the meeting in Copenhagen, explaining that the 1992 ISCB meeting was held on this small and beautiful island, which is easy to get to. The Local Organising Committee aim to bring down the costs and will search for more sponsorship.

5. Any other business

No questions were raised from the floor. The meeting closed at 13:20. Seventy-five ISCB members attended the AGM.

Attendance at the AGM

Theo Stijnen, Hans van Houwelingen, Herald Andersen, Masakazu Iwasaki, Ulrich Mansmann, Bendix Carstensen, Stephen Senn, Fazil Baksh, Anne Whitehead, Jorgen Hilden, Maria Fazekas, Krisztina Boda, Lutz Edler, Martina Mittlboeck, Stephen Walter, Cornelia Enachescu, Denis Enachescu, Barbara S. Hawkins, Stanislav Katina, Corina Violeta Vernic, Urszula Biela, Malgorzata Cwiklinska-Jurkowska, Tsonaka Spyridoulas, Dimitris Rizopoulos, Zdenek Valenta, Kyungmann Kim, Emese Vago, Sandor Kemeny, Erik Cobo, David W Warne, A H Zwindermann, Paul Mulder, Emmanuel Lesaffre, Norbert Victor, Rumana Omar, Midl?Caejwel, Catherine Quantin, Marie Reilly, Vana Sypsa, Giota Touloumi, Lucinda Billingham, Paul Lambert, Walerian Piotrowski, Erik A Sauleau, Marion Proctor, Wolfgang Draxler, Ib Jarle Christensen, Ivan Iachine, Elaine Pascoe, Catherine Klersy, Cornelia Dunger-Baldauf, Robin Prescott, Katherine Lee, Vaclav Fidler, Samuel Manda, Martin Eeg, Maria Grazia Valsecchi, Siem Heisterkamp, Janos Fischer, Vaclav Faltus, Holly Janes, Richard Mowery, Jean-Christophe Thalabard, Ingeborg van der Tweel, Maria Schipper, Ewa Kawalec, Bela Hajtman, Julia Singer, Jenő Reiczigel, Norbert Solymosi, Bjarne Nielsen, Michael Schemper, John Whitehead, Harbajan Chadha-Boreham.

ISCB26 Szeged 2005: Papers for Statistics in Medicine

From Michael Schemper, Chair of the Scientific Programme Committee

After the completion of the conference, 30 papers were submitted to be refereed for inclusion in a special ISCB conference issue of Statistics in Medicine, probably to appear in December 2006.

ISCB Membership and Yahoogroup Emailing List

From Rita Schou (ISCB Office) and David W. Warne (Yahoogroup Administrator)

Did you know we try to make sure our membership database (in Denmark) is kept up to date? We also have an electronic mailing list called iscb@yahogroups.com, which allows members from the current and past year to be contacted to discuss statistical ideas and to receive news about ISCB events. From time to time we compare the 2 databases and if we find you've got 2 email addresses, we'll ask which you prefer.

If you haven't done so already, please send us your email address to allow us to contact you more easily. If you've sent us your email, but haven't accepted the invitation to join the iscb yahoogroup, please accept the next invitation by pressing Reply-Send.

Rest assured that no company will send you any junk email – all emails are checked by the Office or the Yahoogroup Administrator.

ISCB27 Geneva 2006: Conference Awards for Scientists

From Michael Schemper

Conference Awards for Scientists are available for biostatisticians from ISCB target countries (in particular countries of Central and Eastern Europe as well as Third World countries) to attend and present a paper at the 27th ISCB Meeting in Geneva, Switzerland, 27-31 August 2006. Up to six such awards will be granted. An award consists of free accommodation and registration paid by ISCB. Full details of the scheme are given below. Scientists should submit the application form and a one-page summary of the paper to be presented to:

Michael Schemper
 Chairman, ISCB Subcommittee on 'National
 Groups'
 Core Unit for Medical Statistics and
 Informatics, Section of Clinical Biometrics
 Vienna Medical University
 Spitalgasse 23
 A-1090 Vienna, AUSTRIA

Tel: +43 1 40400 6689
 Fax: +43 1 40400 6687
 e-mail: michael.schemper@meduniwien.ac.at

The closing date for application is 15 March 2006.

Rules

1. The ISCB Conference Awards for Scientists

Scheme is administered by the Subcommittee on 'National Groups' established by the Executive Committee of ISCB. The purpose of the scheme is to support and encourage biostatisticians working under financial constraints, and to enable them to participate in international dialogue.

2. Who can apply?

Scientists from 'ISCB target countries' (in particular countries of Central and Eastern Europe as well as Third World countries) whose work will benefit by attending an ISCB conference.

3. What is covered by the award?

The registration fee is waived and inexpensive accommodation is organised and paid for by ISCB. Furthermore, a conference course may be attended free of charge.

4. What are the conditions for application?

Submission of a one-page summary of an intended oral presentation or poster which must concern the application of statistical methodology to clinical or epidemiological research. Applicants who do not have a specialist topic to present are invited to prepare a more general paper with a title such as 'The need for biostatistical development in my country/region/department'. Only one submission per applicant is permissible.

Submission of a completed application form (item 6).

The application has to be received by the Chairman, ISCB Subcommittee on 'National Groups' by 15 March 2006.

5. Who will decide on an application?

The 'National Groups' Subcommittee will decide as soon as possible, usually within six weeks of the closing date for applications, based on the following criteria: Quality of summary, financial need, value of attendance at meeting to region (to National Groups), preference to those not supported by ISCB for the previous meeting, possible set-up of future National Groups. In selecting award winners, each member of the Subcommittee will independently grade each application. In the case of ties in total grades, the Subcommittee will make the final selection through discussion. The Chairman of the Subcommittee will inform each applicant on the Subcommittee's decision.

6. Application form:

**Application
 Conference Awards for Scientists
 27th ISCB Meeting in Geneva, Switzerland, 27-31 August 2006**

First Name	
Surname	
Title	
Country of residence	
Current affiliation (complete address)	
Current position	
Research interests	
Language skills	
I have submitted an abstract (give title)	
Two most relevant publications	
Give details why ISCB should support you to attend this conference	
I would prefer to give an oral presentation / a poster	
I agree to become a member of the ISCB for the year 2006 if I am granted the award. There will be no charge for this.	
Date: _____	Signature: _____

From Marie Reilly

Student Conference Awards are available for registered postgraduate students to attend and present a paper at the 27th ISCB Meeting in Geneva, Switzerland, 27-31 August 2006. It is intended that at least three awards will be made. Selection will be made on the basis of a summary of the paper to be presented, which should illustrate the application of statistical methodology to clinical or epidemiological research. Results of particular studies are of interest only if the analysis has methodological implications or shows a novel and interesting application of biostatistics. Applications, prepared as described below, should be sent to:

Marie Reilly

Chair, ISCB Student Conference Awards Tel: +46 8 5248-3982
Subcommittee Fax: +46 8 31 49 75
Dept. of Medical Epidemiology & Biostatistics email: Marie.Reilly@ki.se
Karolinska Institutet
PO Box 281
Nobels vag 12A
S-171 77 Stockholm
Sweden

The closing date for applications is 15 March 2006.

Rules

ELIGIBILITY:

Any student registered for a postgraduate degree is eligible to apply for an ISCB Student Conference Award, provided they have not been the winner of a previous ISCB Student Conference Award.

The manuscript submitted must relate to original work that has not yet been published, is not the subject of any other award, and is predominantly the student's own work. Acceptable topics encompass all areas of biostatistics, both methodological and applied. However, results of particular studies are of interest only if the analysis has methodological implications or shows a novel and interesting application of biostatistics to clinical or epidemiological research.

Application for a Student Conference Award does not preclude a student from also submitting their abstract to the scientific programme committee, if they so wish.

SUBMISSION PROCEDURE:

Applications should consist of a short abstract of the paper prepared according to the ISCB standard conference format. a summary of the paper of no more than 3 double-spaced pages of 12-point text with a maximum of 3 figures and/or tables on additional pages a statement from the student's supervisor, on official notepaper of the student's institution, confirming that the student is registered for a postgraduate degree, and that the paper to be presented is original, not previously published, not the subject of any other award and is predominantly the student's own work. If the manuscript is co-authored, this letter should also

include an indication of the level of involvement of the various authors. Applications should be received by the Chair of the Awards Subcommittee, no later than 15 March 2006. The items in (a) and (b) must be submitted in electronic format (DOC, PDF or PS format only) to the address given above..

REVIEW:

Applications for Awards will be judged by the Awards Subcommittee, and applicants will be notified of the results as soon as possible, usually within six weeks of the closing date for applications. Judgement will concern the quality of the research described, and its relevance to the application of statistics to clinical and epidemiological research. The presentation of the application documents and the interest of the work to ISCB members will be taken into consideration. The decisions made by the Awards Subcommittee will be final.

In selecting papers for Awards, each member of the Awards Subcommittee will independently grade each paper submitted. In the case of ties in total grades, the Awards Subcommittee will make the final selection through discussion.

Members of the Awards Subcommittee must declare an interest in submissions from students with whom they have had substantial contact. Such contact would certainly include students supervised by or in the same department as Subcommittee members and might also include professional contact with the project as well as family links. The Subcommittee member with an interest in the submission would not grade it, other grades being scaled accordingly, and would not participate in discussions of that submission.

Winning students must be able to travel to the meeting and present their work. For 2006 it is intended to make at least three awards. However, the Awards Subcommittee reserves the right, subject to the approval of the President of the ISCB, to make more or fewer Awards, or even none at all.

AWARDS:

The Award Winners will have their papers scheduled in appropriate Contributed Paper Sessions. Their status as Award Winners will be indicated in the Conference Programme. The ISCB will waive the registration fee of Award Winners, and will pre-pay their hotel accommodation. The ISCB will not pay for any excursions for the student. Normally, it is expected that students will pay for travel, insurance and meals, which expenses will be reimbursed by ISCB, on the basis of appropriate receipts. A fixed per-diem to cover meals will be paid. Full travel costs will be reimbursed, provided that these are incurred economically. Thus full advantage of Apex fares, student discounts and so on should be taken. Adequate insurance cover should be arranged, and will be reimbursed. On being selected, a student must submit a travel budget to the Awards Subcommittee for approval. If it proves more economic to make a longer visit in order to secure bargain fares, the cost of extra accommodation and meals will be borne by the ISCB. Once a budget is approved, additional travel costs will be reimbursed only if a convincing case of their necessity is made.

In the case of hardship, advance payments will be considered. If for good reason a student has to cancel the visit, then the ISCB will consider the reimbursement of costs incurred other than those recoverable from insurance.

Organise an ISCB Conference? Yes, No Problem

The Editor's first ISCB conference was Cambridge, way back in 1993... and that year, Simon Day was kind enough to write an article describing his experiences as chair of the LOC (Local Organising Committee). Have things changed since then? Have we made progress, developed new ideas? Read on...

Simon Day (ISCB News 14, June 1993, ISCB 14)	David Warne (ISCB News 40, December 2005, ISCB 27)
<p>It was Stuart Pocock's big idea in the first place and, to my mind, he has got a lot to answer for. Especially when he declined to be on the Organising Committee, preferring instead to suggest to me in a very flattering way that it was a job better suited to 'a younger man'. Very flattering indeed, Stuart, but my few remaining hairs are going grey! Anyway, I started things off by contacting a few conference organising companies. This is a delicate operation. You have to ask them to put forward their plans for a conference whilst explaining that you have not got any money to pay them and that the ISCB Executive Committee may even decide that they don't want the conference in this country after all. I guess that is a common problem such companies face and I must say I got very helpful comments from several of them.</p>	<p>I have to admit it was all my idea and I can't blame anyone else. The idea started back in 2001 and grew gradually as I explored how a conference could be organised in Geneva for 2005 or 2006 or 2007. Having been to every conference since Simon's in Cambridge, and attended the ExCom meetings since then, I felt I knew what was required, yet realised every meeting is special and no 2 meetings are ever the same. I too started off by contacting an agency who had organised a conference in Geneva with the initial extremely vague idea - and they turned me down. Can't blame them really - what would you say if you were asked to organise something but didn't know when, where or with whom? Yes, getting started is the hardest part, but the agency pointed me in the right direction, namely that of Geneva Tourism, who try to attract conferences to the city. They were a great help in discussing ideas and locations, and sending out the proposal to agencies to bid for.</p>
<p>I first met the people at 'Conference Contact' in April 1991 although my first contact with other companies was back in November 1990 (nearly three years ahead of time! In that April, we made a provisional booking (i.e. one that does not cost anything!) for the conference rooms in the Sidgwick Site at Cambridge after a long walk around many options. Booking a room that will seat 500 and has nearby parallel rooms that seat about 150 each is not easy. In April 1991, we booked the only set of such rooms that Cambridge had available throughout June - October 1993. This is how far in advance everyone else is booking up their conferences so it is obviously important to get going well ahead of time.</p>	<p>So it was in September 2004 that I met the 3 agencies who provided the best offers, and when I had found time to review their offers, Kuoni were chosen, and we re-confirmed the provisional booking of Uni-Mail that Geneva Tourism had made. As Simon pointed out, finding a location for up to 500 people is not so easy even in a city used to running very large exhibitions with up to 100,000 participants. Uni-Mail has the advantage of costing very little when booked through a Geneva University professor. And the date? July and early August are usually rather hot in Geneva and early September has a public holiday on the first Thursday, so the last week in August was chosen. Naturally I checked with ISCB regulars and some local epidemiological people about other conferences and indeed there were some clashes of dates, but this was the best bet.</p>
<p>It was at this time that I began to panic. Were the rooms suitable? Was the cost reasonable? Were the fees being charged by the organising company reasonable? I needed to share the blame for things so appointed the infamous Local Organising Committee. 'Local' is merely a relative term. It means 'based in the same country as the conference will be held'. So who have we got?</p>	<p>So far so good, we had a conference site... now "all" we needed was to find some people for the SPC and LOC, no easy task. My first decision, back in June 2004, to invite Lutz Edler of Heidelberg turned out to be a great success. The email reply came quickly and with enthusiasm, and all our subsequent correspondence has been in the same vein. Since then, mostly by email we've discussed the format of the conference and he's chosen the members of the SPC with an eye to having a broad range of interests and most of the members have been involved in planning sessions. We've also met in Leiden, Geneva, Washington and Szeged: some decisions are much better made face-to-face over a diagram on a piece of paper.</p>
<p>Deborah Ashby said she 'might' be able to help - so I took that as a 'Yes' and asked her to keep an eye on the financial side of things. The budget for the meeting is about £125,000 (excluding accommodation costs) so a constant supply of batteries in her calculator are essential.</p>	<p>Who's involved in the Geneva LOC? There are plenty of statisticians working in the Lac Léman region, but finding ones who wanted to give up their time wasn't so easy...</p>
<p>Tony Johnson said there are lots of statisticians based in Cambridge so it would seem reasonable that some help should be offered to the organisers. Got him too! He is helping me out by providing 'local insight'. He has got a fair idea about where different places are in relation to each other so can offer some advice and confirmation about suitability of conference rooms and accommodation etc. (I live about 150 km from Cambridge and only get there about once a month.)</p>	<p>So I was delighted to recruit Corinne Hager of Nestlé (Sponsorship), Lara Wolfson of WHO (Social programme and WHO session) and John Chapman of Serono (Treasurer). We've met every 2 months over the last year and discussed and reviewed numerous issues and made our suggestions to Kuoni who've been very helpful in advising us.</p>

Organise an ISCB Conference? Yes, No Problem

<p>Alan Phillips does a lot of work for the organisation PSI (Statisticians in the Pharmaceutical Industry) in organising their short courses. He must have about twenty course texts sitting on his book shelf so I gave him a call and asked him what he could come up with. 'International Society of who?' he asked. But his enthusiasm and willingness came through and he agreed to help. I think we have a really interesting and popular group of courses that will appeal to pharmaceutical and academic statisticians. The choice of putting them on the day before the conference rather than the day after was purely driven by availability of rooms but I hope that many of you will feel an extra day in Cambridge could be worthwhile and support these courses.</p>	<p>How to choose courses? Despite ISCB having been around for over a quarter of a century, there are no fixed guidelines, only "tradition" – we usually do it this way, except xx did it that way... So the answer you get depends on who you ask, and it's worth sampling a few past conference organisers to get a balanced picture of what works and what doesn't. In the case of courses, it was a mixture of proposals from ISCB experts and ideas of courses I'd like to attend and would appreciate. We're hopeful the courses will be a great success as this aspect of the conference has really established itself in recent years as a highlight of the week. Book early to avoid disappointment – places are limited to retain a workshop atmosphere in which questions can be discussed.</p>
<p>And then there is me. I once heard someone say that the chairman of anything shouldn't have to do too much - just make a lot of noise and enthuse others to do things. Maybe I don't delegate enough... I certainly get everything done by my team (of 'younger men') that I ask of them... but I still end up with A LOT to do.</p>	<p>Yes, as any manager will tell you, delegation is not easy, and ultimately someone has to make a decision. But it has been a pleasure working with the LOC and SPC chair and things seem to be falling nicely into place. A LOT to do maybe an understatement... at times I've wondered if I could manage, and at others, there's time for a rest as a big deadline has been met. The critical times are those leading up to publishing the 1st announcement and the Brochure, and the latter should mark the point where it's clear to all that the conference will definitely take place and how it'll look and feel.</p>
<p>Of course, no-one cares about the things that go on behind the scenes. What everyone really wants to know about is the scientific programme. I'm not sure how Doug Altman's name got put forward. That may have been engineered into the same conversation I originally had with Stuart Pocock. When I asked Doug if he would chair the Programme Committee he was not sure. He had all sorts of other commitments and wanted to think about it for a while. A while later I found some excuse to call him and broached the subject again. His response was something like '... of course I'll do it. I really ought to say "No" but you know how it is with these things'. 'Good', I thought: Got him! We started talking about who should be on the Scientific Programme Committee and I said that it was important that there is close liaison between him and the Organising Committee. 'Right', he said, 'you walked into that one, didn't you?'. I was his first recruit.</p>	<p>Yes, I never really cared about the things that went on behind the scenes – I just noted the very few things which weren't perfect at each conference... and of course you may spot some mistakes in GE06. To go back a little and review my choice of SPC chair, Lutz and I had almost worked together in Heidelberg back in the summer of '89 when I was a research student looking for a summer somewhere different... in the end I had a great time in the fine German city of... Düsseldorf! It wasn't for another 10 years that I reached Heidelberg for ISCB 20, a meeting for which I thought the scientific organisation was outstanding, which contributed to my choice of Lutz. I can see we won't be disappointed for that of ISCB 27. Finally, I was delighted to be nominated as Co-Chair of the SPC, which reflects Lutz and my cooperation in the organisation – we both need to know how the organisation of the other's work is going.</p>
<p>Doug and I pondered friends, enemies and useful contacts. Choosing a committee to work with is a great way to regain contact with past colleagues or to get to know people better with whom you have never had much to do with but have often wanted to work. We were biased towards the UK simply because the conference is to be held here, but were also conscious of trying to get good international representation (a point that proved particularly important later on). Unlike the Local Organising Committee, I cannot begin to describe the process by which each name was decided upon - it was a very multivariate decision - but the list we ended up with is as follows: Doug, myself, Per Kragh Andersen, Mike Campbell, Giuseppe Gallus, Nancy Geller, David Machin, Martin Schumacher, Stephen Senn, Hans Wedel and Andreas Zipfelf.</p>	<p>Lutz did most of the recruiting, but once again he was kind enough to check each proposal with me. There's a great temptation to choose experts who've done it all before, yet at the same time we're aware ISCB has to evolve and get newcomers involved, perhaps introducing new topics never covered before, and then there are local considerations. In this way, some names came from each of these approaches, and the final SPC is as follows: Lutz Edler (Chair, D), ·David W. Warne (Co-Chair, CH), ·Per Kragh Andersen (DK), Elia Biganzoli (I), Klaus Dietz (D), Diego Kuonen (CH), ·Peter Lachenbruch (USA), Andre Langaney (CH), Emmanuel Lesaffre (B), ·Mats Lörstad (S), ·Gerd Rosenkranz (CH), ·Patrick Royston (UK), Sue Todd (UK) ·and Maria-Pia Victoria-Feser (CH).</p>

Organise an ISCB Conference? Yes, No Problem

<p>Deciding on topics was the first task of the Programme Committee whilst the Organising Committee was frantically trying to get the Call for Papers finalised and distributed. We needed to decide on themes to publish there. That was not so difficult, although a lot of care and thought was put into it. Having recently made a move from academia to industry I am acutely aware of the different needs and interests of the two groups and wanted to ensure the Conference would be equally interesting to both groups. Hence, we picked topics such as Statistics, Medicine and the Law. This is important in public health issues and in pharmaceutical liability cases, as well as simply being fascinating in its own right. We picked the topic of Measurement and Evaluation of Risk Factors, which is important to epidemiologists and clinical trialists alike. Each topic was carefully thought about and we hope virtually all of them will be useful to all delegates - and if not directly useful, then certainly very interesting.</p>	<p>The format of GE06 differs from most recent conferences in that the traditional mini-symposium has been replaced by 5 "Special" sessions of particular interest to Geneva. We will see how this works. We decided that choosing topics for the Invited and Special sessions had to be done early in order to shape the conference, and this was completed around May 2005 in time for printing the 1st announcement to be sent out with the June 2005 News. This gave us something to show to the world, and was a starting point for getting the contents of those sessions ready by November 2005 for the December News. Choosing themes or preferred topics is an idea which has been done for some ISCB conferences, but not that many. Why did we do it? Again, we wanted to shape the conference in advance and hope to receive top quality contributed papers based on these topics which can be grouped together to produce excellent contributed sessions. Of course papers on all other topics are most welcome as well.</p>
<p>Deciding on who to invite was difficult. Again, a very multivariate decision: trying to balance countries (and hence potential travel costs) was important. Naturally, some topics had dozens of potential speakers, others very few. Here we have made a great deal of use of the Programme Committee members. They are the ones who know best about the people in their countries - or are in a position to find out - so there were a lot of faxes back and forth between the various Committee members regarding specific individuals.</p>	<p>This is where our SPC has exceeded our expectations. Each session has 1 or 2 organisers and they have quietly done a great job in building sessions based on quite brief scientific and logistical instructions from Lutz and me. My fax machine died this year and was not replaced! And letters - I looked back to see we used to send these to ask each other questions... ah, the good old days! E-mail has certainly made contacting people much quicker, but it doesn't remove the communication difficulties entirely as negotiation is still needed. Which were the trickiest sessions to organise? I'd say it was those where there were too many ideas!</p>
<p>We also wanted to wait for some of the submitted Abstracts to arrive to see what you wanted to talk about. A couple that arrived early and looked particularly interesting we reviewed and considered worth 'upgrading' to invited papers. Maybe if next year's organisers do the same it will be an incentive to submit early. The Local Organisers were, meanwhile, busy preparing the Call for Registration and wanted as much detail of the programme and invited speakers as was possible from the Programme team.</p>	<p>We have similar ideas for good contributed papers - some may be put in sessions which follow on from the Invited and Special sessions, in order to further develop the themes. Please keep an eye on the website, www.iscb2006.info for developments, especially from June 2006 when the contributed part of the Scientific Programme will take shape. Talking of the web, when did ISCB first have one? Was it Heidelberg 1999? This is still a relatively new concept and one which didn't exist in the days of ISCB 14. For Geneva 2006, in fact we have 2 sites, one in Geneva for the local logistical details, and another in Heidelberg for the Scientific programme, including submitting abstracts. Thanks to Lutz for recruiting Axel Benner to be the webmaster for the latter.</p>
<p>Waiting for the Abstracts to arrive in the post was a little nerve-wracking. You may recall the deadline for submissions was 1st March.... by the first week of February we only had five Abstracts submitted! Where were you all? We have ended up with about 130 in total, many of which will have to be rejected through lack of time in the programme. This is the wrong reason for rejecting some very good and interesting work. But I don't think I could organise a ten day conference!</p>	<p>I'm writing this article for the December News rather than the June News just before the conference, so this waiting period has yet to start. Lutz and I are really looking forward to seeing the abstracts arrive. Lutz and the SPC will process the abstracts and I'll be trying to arrange them into a sensible order in the conference programme.</p>
<p>Doug has sent each of the Abstracts to two of the Programme Committee to review and make a recommendation. In addition, he and I have each read them all and formed opinions. How did we decide which to accept and which to reject? It will be difficult not least because it is not simply a question of ranking them on scientific merit. We need a balance in the programme and we feel inclined towards a variety of presenters rather than the same faces cropping up too often: so if you are one of the people who submitted a handful of Abstracts, thanks, but I expect we will not accept them all - however good they are.</p>	<p>I think a similar process is used in most ISCB conferences for reviewing the abstracts. Assuming most will be of a high standard, something I'm told is usually the case, the hard part is choosing the best of the best and organising them into sessions. Occasionally excellent papers will appear as posters, and we want to emphasise the importance of posters. Time will be set aside for poster presentations and there will be a small competition for the best posters. As Simon said, we will try to avoid having the same speakers appearing too many times, and certainly not having the same person speaking in 2 sessions at the same time!</p>

Organise an ISCB Conference? Yes, No Problem

<p>So what next? My hope is that things should go quiet for a while now. All that should happen is that your cheques should start arriving stating your willingness and enthusiasm to attend the conference. I would put in a plea for you to register early. At the very least it will help tremendously with cash flow. We have already received over £5000 in sponsorship money and 'borrowed' over £10,000 from the Society - and spent the lot! So before we have to borrow much more, some of your registration fees would really help.</p>	<p>I too am hoping for a few quiet weeks... The conference trial design is complete, and we now have to run it according to the protocol and analyse the scientific and financial results at the end to see what we can learn for future conferences and pass this information on to the subcommittee on Conference Organising and the chairs of the next 2 conferences in Alexandroupolis and Copenhagen. Talking of money, cheques have gone the way of letters and faxes to be replaced by credit cards and bank transfers. No money has been borrowed from the Society as costs have been generously covered by Geneva Tourism for the 1st announcement and we should soon start receiving sponsorship money.</p>
<p>Apart from waiting to receive money from you, our next task is to prepare and print the final timetable of sessions and the programme with all the Abstracts and additional information. We have used previous years' publicity material as a guide to what we should produce and I suspect we will use the layout and style of previous Programmes to design ours. The proof reading is a task that I do not relish.</p>	<p>Previous conferences have again varied the way the final programme was presented. In some, everything was in one large book, in others it was divided into an Abstracts Book and a smaller Final Programme, and it's the latter approach we've chosen to match the division of responsibilities between Heidelberg and Geneva.</p>
<p>So that is about all there is to it, really. Why not offer to organise one yourself? You don't have to wait until you are asked. You get to know lots of people although it does take up a lot of time. Sufficient time, in fact, that I need to put in a big 'Thank You' to my boss for supporting me throughout all of this (promise I'll do some work next year!) and my wife (promise I'll decorate the house next year! Thanks also go to the rest of my Local Organising Committee, the Programme Committee and all their respective employers who are supporting them by giving their time. Further thanks to Peter, Cathy and the other staff at 'Conference Contact'.</p>	<p>So after reading our accounts, would I recommend organising a conference to anyone? It's been a great experience, at times exhausting, sometimes challenging and always full of opportunities to negotiate. Overall, I'd say if you have a good feeling of how ISCB conferences run, are willing to seek and follow advice, and are not afraid of details or innovation, Go for it! Thanks to my wife for her patience with me, and our growing toddler who arrived last year and has already been to his first conference in Leiden. I'm very grateful for the help of the LOC and Kuoni, Steeve Girod and Nathalie Courtine, Lutz and the SPC, as well as previous organisers of the conferences in Trento, Dijon, Leiden and Szeged, and the ISCB Officers with their patience and advice as the germ of an idea has grown.</p>
<p>And finally, it is not too early to acknowledge the sponsorship being offered to us (cash or otherwise) by Lilly Research Ltd, PSI (Statisticians in the Pharmaceutical Industry), Roche Products Ltd, The Royal Statistical Society, Scotia Pharmaceuticals Ltd, Spadille Biostatistik ApS, Sterling Winthrop Research and The Wellcome Foundation. I shall repeat these words of thanks as often as I feel I can get away with it. Until we know how many people plan to attend the meeting, we cannot know how much to charge. If we do not make the break-even number of participants then the Conference will make a loss and ISCB will have to make up the difference. That would be embarrassing! If anyone else who reads this works for a company who may wish to offer some kind of sponsorship to the meeting then I would be very pleased if you called me to discuss any options.</p>	<p>At the time of writing, we have one definite sponsor, of the Special session on Dental Statistics, and a lot of interest from potential supporters. We've already had several requests from companies wanting to exhibit at the conference, which is very encouraging, especially as the Advertising, Sponsoring and Exhibition Brochure will only be sent out in December. If you think your company would like to sponsor us, or to advertise or to exhibit at the conference, please contact Kuoni. We're quietly confident of a large number of participants and it would be in your company's interests. To end this financial section, I should mention the help we've received from the Officers in reviewing the Kuoni contract and budget and the overall budget. It's reassuring to know we're following the guidelines.</p>
<p>I hope to see as many of you in Cambridge as are able to come.</p>	<p>I hope to see many old and new faces in Geneva and in Alexandroupolis and in Copenhagen and all the conferences to come.</p>

Books for Review by Harry Southworth

Books for review:			
Author(s)	Title	Publisher (year) ISBN	Reviewer
1. Byron Jones and Michael G. Kenward	Design and Analysis of Cross-Over Trials (Second Edition)	Chapman & Hall/CRC, (2003) 0-412-6-640-2	
2. Daniel Zelterman	Discrete Distributions: Applications in the Health Sciences	Wiley (2004) 0-470-86888-0	
3. David Collett	Modelling Survival Data in Medical Research (Second Edition)	Chapman & Hall/CRC, (2003) 1-58488-325-1	
4. David J. Spiegelhalter, Keith R. Abrams and Jonathan P. Myles	Bayesian Approaches to Clinical Trials and Health-care Evaluation	Wiley (2003) 0-471-49975-7	
5. Eric Stallard, Kenneth G Manton and Joel E Cohen	Forecasting Product Liability Claims: Epidemiology and modeling in the Manville Asbestos Case	Springer (2005) 0-387-94987-9	
6. Frank R. Hampel, Elvezio M. Ronchetti, Peter J. Rousseeuw and Werner A. Stahel	Robust Statistics: The Approach Based on Influence Functions	Wiley (2005) 0-471-73577-9	
7. Geoffrey McLachlan and David Peel	Finite Mixture Models	Wiley (2000) 0-471-00626-2	
8. George A. F. Seber and Alan J. Lee	Linear Regression Analysis (Second Edition)	Wiley (2003) 0-471-41540-5	
9. George E. P. Box, J. Stuart Hunter and William G. Hunter	Statistics for Experimenters (Second Edition)	Wiley (2005) 0-471-71813-0	
10. Jean Dickinson Gibbons and Subhabrata Chakraborti	Nonparametric Statistical Inference (Fourth Edition)	Chapman & Hall/CRC, (2003) 0-8247-4052-1	
11. Julian J. Faraway	Linear Models with R	Chapman & Hall/CRC, (2005) 1-58488-425-8	
12. M. M. Desu and D. Raghavarao	Nonparametric Statistical Methods for Complete and Censored Data	Chapman & Hall/CRC, (2004) 1-58488-319-7	
13. Mark Woodward	Epidemiology: Study Design and Data Analysis (Second Edition)	Chapman & Hall/CRC, (2005) 1-58488-415-0	
14. Murray Aitkin, Brian Francis and John Hinde	Statistical Modelling in GLIM 4	Oxford (2005) 0-19-852413-7	
15. Phillip Good	Permutation, Parametric, and Bootstrap Tests of Hypotheses (Third Edition)	Springer (2005) 0-387-20279-X	
16. Rasmus Nielsen (Editor)	Statistical Methods in Molecular Evolution	Springer (2005) 0-387-22333-9	
17. Robert E. Weiss	Modeling Longitudinal Data	Springer (2005) 0-387-40271-3	
18. Shein-Chung Chow, Jun Shao and Hansheng Wang	Sample Size Calculations in Clinical Research	CRC (2003) 0-8247-0970-5	
19. Tomasz Burzykowski, Geert Molenberghs and Marc Buyse (Editors)	The Evaluation of Surrogate Endpoints	Springer (2005) 0-387-20277-3	
20. Vance W. Berger	Selection Bias and Covariate Imbalances in Randomized Clinical Trials	Wiley (2005) 0-470-86362-5	
21. Warren J. Ewens and Gregory R. Grant	Statistical Methods in Bioinformatics: An Introduction	Springer, (2005) 0-387-40082-6	

Books reviews in this issue:

Author(s)	Title	Publisher (year) ISBN	Reviewer
1. Lemuel A Moyé	Multiple Analyses in Clinical Trials	Springer [2003] 0-387-00727-X	Francois Aubin, France
2. Geoffrey J. McLachlan	Discriminant Analysis and Statistical Pattern Recognition	Wiley (2004) 0-471-69115-1	Denis Enachescu, Romania
3. Andrew B. Lawson et al	Disease Mapping with WinBUGS and MLwiN	John Wiley [2003]	Maciej Gorkiewicz, Poland
4. Margaret Sullivan Pepe	The Statistical Evaluation of Medical Tests for Classification and Prediction	Oxford (2003) 0-19-850984-7	Jacques Jamart, Belgium
5. Sylvia Wassertheil-Smoller	Biostatistics and Epidemiology (3rd edn)	Springer (2003) 0-387-40292-6	Faans Steyn, South Africa
6. G. A. F. Seber and C. J. Wild	Nonlinear Regression	Wiley (2003) 0-471-47135-6	Corina Violeta Vernic, Romania
7. Harvey Motulsky and Arthur Christopoulos	Fitting models to biological data using linear and nonlinear regression	Oxford (2004) 0-19-517180-2	Tiberiu Postelnicu, Romania
8. Stephanie Green, Jacqueline Benedetti and John Crowley	Clinical Trials in Oncology (Second Edition)	Chapman & Hall/CRC (2002) 1-58488-302-2	Vana Sypsa

Books for Review (continued)

Books recently sent for review:			
Author(s)	Title	Publisher (year) ISBN	Reviewer
9. Daniel Sorensen and Daniel Gianola	Likelihood, Bayesian, and MCMC Methods in Quantitative Genetics	Springer (2002) 0-387-95440-6	Sada Nand Dwivedi
10. David A. Belsley, Edwin Kuh and Roy E. Welsch	Regression Diagnostics	Wiley (2004) 0-471-69117-8	Ulrich Mansmann, Germany
11. Eric Vittinghoff, David V. Glidden, Stephen C. Shiboski and Charles E. McCulloch	Regression Methods in Biostatistics: Linear, Logistic, Survival and Repeated Measures Models	Springer (2005) 0-387-20275-7	Rainer Muche
12. Ettore Marubini and Maria Grazia Valsecchi	Analysing Survival Data from Clinical Trials and Observational Studies	Wiley (1995) 0-470-09341-2	Andreas Wienke
13. George A. F. Seber	Multivariate Observations	Wiley (2004) 0-471-69121-6	Elzbieta Pleszczyńska, Poland
14. George G. Woodworth	Biostatistics: A Bayesian Introduction	Wiley (2004) 0-471-46842-8	Victor Moreno
15. Gerlad van Belle, Lloyd D. Fisher, Patrick J. Heagerty and Thomas Lumley	Biostatistics: A Methodology for the Health Sciences (Second Edition)	Wiley (2004) 0-471-46842-8	Richard Kay
16. J M Bernardo et al (eds.)	Bayesian Statistics 7	Oxford University Press (2003) 0-19-852615-6	Stefan Tigan, Romania
17. J. Edward Jackson	A User's Guide to Principle Components	Wiley (2003) 0-471-47134-8	Nicole Close, USA
18. John Aitchison, Jim W. Kay and Ian J. Lauder	Statistical Concepts and Applications in Clinical Medicine	Chapman & Hall/CRC (2005) 1-58488-208-5	Denis Enachescu
19. John P. Klein and Melvin L. Moeschberger	Survival Analysis: Techniques for Censored and Truncated Data	Springer (2003). 0-387-95399-X	Sarah White, Malawi
20. John Verzani	Using R for Introductory Statistics	Chapman & Hall/CRC (2005) 1-58488-450-9	Justin Clayton
21. Marc Aerts, Helena Geys, Geert Molenberghs and Louise M. Ryan	Topics in Modelling of Clustered Data	Chapman & Hall/CRC (2002) 1-58488-185-2	S.H. Heisterkamp, Netherlands
22. Richard M Heiberger	Statistical Analysis and Data Display: An Intermediate Course with Examples in SPLUS, R and SAS	Burt Holland (2004) 0-387-40270-5	Gaj Vidmar, Slovenia

Books sent for review a long time ago

Author(s)	Title	Publisher (year)	Reviewer
1. Allen Cato, Lynda Sutton, Allen Cato III (eds)	Clinical Drug Trials and Tribulations (2 nd ed)	Marcel-Dekker (2002) 0-8247-0314-6	Axel Hinke
2. CF Jeff Wu & Michael Hamada	Experiments: Planning, Analysis, and Parameter Design Optimisation	John Wiley (2000)	Gilg Seeber
3. Donald C Monkhouse & CT Rhodes (Eds.)	Drug Products for Clinical Trials	Marcel Dekker (1998)	Koos Lubsen
4. Kirkwood	Essentials of Medical Statistics	Blackwell	Dick Bezemer
5. Martin J Crowder	Classical Competing Risks	Chapman&Hall/CRC (2001) 1-59488-175-5	Dario Gregori
6. Michael Finkelstein, Bruce Levin	Statistics for Lawyers (2 nd ed.)	Springer (2001) 0-387-95007-9	David A. Sclar
7. Michael Healy	Matrices for Statistics	Oxford (2000)	Istvan Janosi
8. Peter Armitage (ed)	Encyclopedia of Biostatistics: Vol. 4: Med-Pre	John Wiley (1998)	Aurelio Tobias
9. Shein-Chung Chow & Jen-Pei Liu	Design and Analysis of Bioavailability and Bioequivalence Studies	Marcel-Dekker (2000)	Graham Kimber

Book publishers' webpages:

Arnold	http://www.arnoldpublishers.com/
Blackwell	http://www.medirect.com/
Cambridge University Press	http://publishing.cambridge.org/stm/mathematics/stats/
Chapman & Hall, CRC	http://www.crcpress.com/shopping_cart/categories/categories_products.asp?parent_id=104
Marcel Dekker	http://www.dekker.com/catalog/search.jsp?category=%2FStatistics
Oxford University Press	http://www4.oup.co.uk/
Springer	http://www.springer.de/statistic/books/newbooks.html
John Wiley & Sons	http://catalog.wiley.com/

Important note to potential reviewers:

We regularly receive books from publishers for review in the Newsletter. We are most grateful for these "donations", the reviews of which we regard as a service to you, our members. Regretfully, some individuals, despite repeated reminders, neither return a review, nor the book to ISCB... When requesting a book, please remember that you're making a commitment to the Society to do a little work in return for keeping the book.

Please do a little work in return for keeping the book and your name will be published in the News!

For the format and length, please see recent issues of ISCB News. You can send the review in a variety of formats but plain text email, html, RTF or Word are preferred. The reviews may be edited for clarity (English grammar and spelling, punctuation etc.).

This book is published by Springer in their "Statistics for Biology and Health" series. According to the author, the aim of the book is to address the issue in a manner devoid of mathematical complexity. The targeted readers are advanced medical students, clinical investigators at all levels, research groups within the pharmaceutical industry, regulators at the local, state, and federal levels, and junior biostatisticians. The book consists of an introductory section, 14 chapters, and 5 appendices. The introductory section, entitled *Blossoms on a Healthy Plant*, discusses the respective roles and contribution of biostatistics and epidemiology in clinical research and clinical trial principles. Chapter 1, *Fundamentals of Clinical Trial Design*, gives an overall review of principles underlying the design of clinical trials (covering the issues of randomisation, blinding, interim monitoring, intention to treat analyses, measurement of effect, hypothesis testing, sampling error and significance testing, power and sample size computation). Chapter 2, *Multiple analyses and the Random Experiment*, presents the fundamental importance of prospective planning of the statistical analyses of a clinical trial and the misleading trap of conclusions based on post-hoc, data-driven analyses. Chapter 3, *The Lure and Complexity of Multiple Analyses*, introduces the subject of multiple analyses: why do we perform multiple analyses? (multiple endpoints, multiple time points, multiple treatment arms, subgroup analyses); what are the consequences?; how to control the type one error rate? Chapters 4 to 6 address the issue of multiple endpoints analysis in a two treatment-arms clinical trial. Chapter 4, *Multiple Analyses and Multiple Endpoints*, focuses on the analysis of multiple independent endpoints and proposes a strategy for analysis: triage of endpoints (primary/secondary/exploratory), and allocation of type I error. Chapter 5, *Introduction to Multiple Dependent Analyses I*, and chapter 6, *Multiple Dependent Analyses II*, extend the approach to the cases where the analyses are not independent, with the introduction of a dependency parameter. The case of two dependent analyses being addressed in chapter 5, while chapter 6 generalizes the discussion to more than two analyses. Chapter 7 and 8 discuss the notion of composite endpoints. Chapter 7, *Introduction to Composite Endpoints*, introduces the notion, discusses the complications involved in the construction of composite endpoints, and the notion of homogeneity/heterogeneity of treatment effect between individual components of the composite endpoint. The combined endpoint must be broad while simultaneously retaining its interpretability, a property called "coherence" by the author. Chapter 8, *Multiple analyses and Composite Endpoints*, then discusses the analysis of composite endpoints. The combined use of prospective allocation of type I error and measure of dependency between analyses allows the analysis of therapy effect on both

the composite endpoint and some (or all) of its components.

The issue of subgroup analyses is then covered in chapters 9, *Introduction to Subgroup analyses*, 10, *Subgroups II: effect Domination and Controversy*, and 11, *Subgroups III: Confirmatory Analyses*. The distinction must be made between a subgroup analysis that compares the effect of an intervention across subgroup strata and an analysis which seeks to confirm the efficacy of therapy within a single subgroup stratum. The reader is clearly warned that, in the absence of prospectively defined confirmatory subgroup analyses, the best estimate of the effect of a randomly allocated therapy within a subgroup stratum is the effect of that therapy on the overall cohort (effect domination). Disciplined, prospectively planned analyses, on relevant subgroups (i.e. subgroups with a biologically plausible rationale) with adequate allocation of type I error and possibly adjustment of the overall sample size of the trial can be defined as confirmatory.

Chapter 12, *Multiple Analyses and Multiple Treatment Arms*, examines the analysis of clinical trials when there are several treatment groups in addition to the control group.

Finally, Chapter 13, *Combining Multiple Analyses*, introduces the reader to the design of complex clinical trials. Differential type I error allocation, combined endpoints and confirmatory subgroup analyses can be prospectively combined into effective clinical trials designs.

Chapter 14, *Conclusions: The Two-Front War*, is a final conclusive text, reminding the reader that the design of a clinical trial is a compromise between the legitimate temptation to make the research effort as productive as possible, leading to the multiplication of endpoints and potential analyses, and the need of a sound and rational scientific statistical approach, based on prospective endpoint triage and type I error control.

All the chapters of the book are richly illustrated by real examples from the medical literature, helping the reader to progress in his understanding of the issues presented. Each subject is presented in a progressive manner, moving from the simpler issues to the more complex ones.

This book is clearly well adapted to its targeted audience. Devoid of any complex mathematical or statistical developments, it is to be recommended to all "non statistical" personnel involved in clinical trials design or interpretation (clinical investigators, clinical researchers in the pharmaceutical industry, regulators, etc.) but also to junior biostatisticians wishing to have a comprehensive introduction to the issue of multiplicity in clinical trials.

Discriminant Analysis and Statistical Pattern recognition provides a systematic account of the subject. The book can be used as a source of reference in work of either a practical or theoretical nature on discriminant analysis and statistical pattern recognition. To this end, an attempt has been made to provide a broad coverage of the results in these fields. It is assumed that the reader has a fair mathematical or statistical background. The book consists of thirteen chapters and the material is well written, clear and concise. The book provides an excellent source of reference material; over 1200 references are given. There are many examples from medicine, including detection of haemophilia A carriers, statistical diagnosis of diabetes, case study of renal venous rennin in hypertension, differential diagnosis of some liver diseases and a whole chapter dedicated to statistical image analysis.

Concerning the coverage of the individual chapters, Chapter 1 provides a general introduction to discriminant analysis. In Chapter 2, likelihood-based approaches to discrimination are considered in a general context. This chapter also provides an account of the use of the EM algorithm in those situations where maximum likelihood estimation of the group-conditional distributions is to be carried out using unclassified feature data in conjunction with the training feature data of known group origin.

As with other multivariate statistical techniques, the assumption of multivariate normality provides a convenient way of specifying a parametric group structure. Chapter 3 concentrates on discrimination via normal theory based models. In the latter part, the author considers the reduction of the dimension of the feature vector through linear projections that optimise certain separatory and allocatory measures for normal models.

In Chapter 4, the author considers available results for the distribution of discriminant functions and associated rules of allocation in the case of multivariate normal group-conditional distributions for which the parameters may or may not be known. He considers also for these models distributional results for the conditional error rates of sample-based rules, in particular of the plug-in sample version of the Bayes rule. Analytical results are available only in special cases such as for $g = 2$ homoscedastic groups.

Chapter 5 concentrates on some problems that arise with the estimation of normal theory based discriminant rules in practical situations. One problem to be addressed is that of discriminant rules formed from estimates with too much variability, which arises in fitting models with too many parameters

relative to the size of the available training sample. Other problems to be considered in this chapter concern the performance of the sample normal based linear and quadratic rules under departures from normality, and robust estimation of discriminant rules. The regularized discriminant analysis approach is emphasized there.

Chapter 6 is concerned primarily with data analytic considerations with normal based discriminant analysis. With a parametric formulation of problems in discriminant analysis, there are a number of preliminary items to be addressed. They include the detection of apparent outliers among the training sample, the question of model fit for the group-conditional distributions, the use of data-based transformations to achieve approximate normality and the assessment of typicality of the feature vector on an unclassified entity to be allocated to one of the specified groups. In the second half of the chapter, attention is devoted to the graphical representation of the feature data on the classified entities in the training set. As the human capacity for pattern recognition is limited to low dimension, highly revealing low-dimensional representations of the feature data are required if much light is to be shed on such matters as the underlying group structure. At the end of the chapter, the author presents some examples of discriminant analyses in less than straightforward situations, including a case in which there is not an unequivocal classification of the training data with respect to the underlying groups and a case in which there is some doubt as to the actual group structure. Problems of this type, which are on the interface of discriminant and cluster analyses, occur frequently in practice and can be difficult to handle.

Chapter 7 consider the use of non-normal models to fit the group-conditional distributions of the feature vector in the parametric construction of discriminant rules. The case in which all the feature variables are discrete is to be considered first. The parametric models to be considered in the discrete case can be viewed as attempts to smooth the nonparametric estimates obtained with the multinomial model. In the case of mixed feature variables in which some are discrete and some are continuous, the author highlights the role of the location model. It assumes that within each group, the continuous feature variables have a multivariate normal distribution with a common covariance matrix, conditional on each distinct realization of the discrete feature variables. Finally in this chapter, a brief account is given of some non-normal models that have been adopted for

discrimination in the case of all continuous feature variables.

A semi-parametric approach is adopted in Chapter 8 with a study of the widely used logistic model for discrimination. Nonparametric approaches to discrimination are presented in Chapter 9. Particular attention in this chapter is given to kernel discriminant analysis, where the nonparametric kernel method is used to estimate the group-conditional densities in the formation of the posterior probabilities of group membership and the consequent discriminant rule.

Chapter 10 is devoted fully to the important but difficult problem of assessing the various error rates of a sample-based discriminant rule on the basis of the same data used in its construction. The error rates are useful in summarizing the global performance of a discriminant rule. Of course, for a specific case as, for example, in medical diagnosis, it is more appropriate to concentrate on the estimation of the posterior probabilities of group membership. Accordingly, a separate chapter (Chapter 11) is devoted to this problem.

Chapter 12 is on the selection of suitable feature variables using a variety of criteria. This is a fundamental problem in discriminant analysis, as there are many practical and theoretical reasons for not using all of the available feature variables. Finally, Chapter 13 is devoted to the statistical analysis of image data. Here the focus is on how to form contextual allocation rules that offer improved performance over the classical non-contextual rules, which ignore the spatial dependence between neighbouring images.

The book is a monograph, not a textbook. It should appeal to both applied and theoretical statisticians, as well as to investigators working in the many diverse areas in which relevant use can be made of discriminant techniques. The book contains an extensive subject index.

Among the advances covered are regularized discriminant analysis and bootstrap-based assessment of the performance of a sample-based discriminant rule and extensions of discriminant analysis motivated by problems in statistical image analysis. Unfortunately important advances like neural networks, support vector machines and flexible discriminants are missing from the monograph, as are French and Russian references.

In conclusion, I recommend this book. It makes a worthwhile addition to any statistics library.

Andrew B. Lawson, William J. Browne, Carmen L. Vidal Rodeiro

Disease Mapping with WinBUGS and MLwiN

Wiley (2003) 0-470-85604-1

This book complements the Wiley series on Statistics in Practice, which is aimed by its editors to provide well-written workbooks for researchers both in higher education and beyond, across broad subject areas. Such books are particularly welcoming by final-year undergraduate and graduate level students of statistics and other applied sciences.

The book is organized into 10 chapters. Let us start our review from the fourth chapter 'WinBUGS' and fifth one 'MLwiN basis'. The Authors, Lawson, Browne and Vidal Rodeiro, advocate there the learning by doing approach. So, they begin with necessary practical information: the BUGS software (Bayesian inference Using Gibbs Sampling) can be downloaded from the website <http://.mrc-bsu.cam.ac.uk/bugs/> owned by Medical Research Council (MRC) Biostatistics Unit, Cambridge, UK. There also, the free restricted version and WinBUGS Manual (Spiegelhalter et al, 2002) are available. Then, step by step, the authors introduce us to how to start work with WinBUGS, how to specify the model using graphical modeling or text-based BUGS language, and how to introduce the data. Among other practical advice, a separate section with four figures discusses how to carry out convergence diagnostic and statistical and graphical analysis of the Monte Carlo sampling output. At the end of fourth chapter the use of GeoBUGS, an add-on module to WinBUGS, is explained.

The fifth chapter has similar organization. First, there is advice that all software and two user's guides, by Rasbach et al. (2000) and by Browne (2003) can be downloaded from the host <http://multilevel.ioe.ac.uk>. It is mentioned, that MLwiN is not freely available, but that it attempts to be accessible to researchers whose somewhat limited statistical knowledge may make WinBUGS too difficult or bothersome for them. Above all, the nice feature of MLwiN is that it uses a worksheet file format so one can easily read or simply copy and paste data stored in other formats, such as Excel. Nevertheless, several another ways to input data, create new variables and plot them are explained with

accompanying use of 10 figures. The next 18 figures support explanations on fitting standard hierarchical models but starting from single-level Poisson regression models. After that, these examples are completed with use of MCMC estimation and explained with 11 figures. The last 9 figures in the fifth chapter illustrate two common methods for spatial modeling: the multiple-membership models and the CAR models.

The core chapters of this book, namely the sixth, *Relative Risk Estimation*, and seventh, *Focused Clustering: the Analysis of Putative Health Hazards*, are both constructed to encourage experimentation and can be easily adapted to individual research.

There, two real-life data sets are step by step analysed. The problem of defining the models and estimating their parameters is expressed in a laconic but clear mathematical form. The listings of the used macros are included into text and then collected into Appendix 1, *WinBUGS Code for Focused Clustering Models*. There are 9 macros the for so named Falkirk example and 5 macros for the Ohio example. As above, all analyses are supported with a lot of very informative figures. In result, the concisely written chapters 4-5 and 6-7 become highly accessible, especially as they are designed for a very specific audience.

For some readers the next two chapters will be of a grater interest. The eighth, *Ecological Analysis* is organized in the same way as the core chapters. There, four WinBUGS scripts are listened, the used equations are cited and explained thoroughly, but the main emphasis is on applied aspects. The ninth chapter, *Spatially-correlated Survival Analysis*, looks somewhat sparse, but the WinBUGS code is available at <http://www.biostat.umn.edu/brad> for a range of models. Nevertheless, it seems that the users not familiar with WinBUGS should start with simple examples from the fourth chapter and then progress to more complex ones.

It should be noted that this book is much more than a manual for choice of the proper computing procedures or guidance on how to proceed with model-based relative risk estimation.

The authors' intent is to provide a single source for both the basic theory behind disease mapping techniques and their practical implementation in WinBUGS and MLwiN. In the first chapter, *Disease Mapping Basics*, they briefly introduce the earlier, but still valid, not full Bayesian methods. Then, in chapters 2, *Bayesian Hierarchical Modeling*, and 3, *Multilevel modeling*, they provide general background to these approaches in relation to disease mapping applications. The section, *Notation*, on specific terminology used in this book is placed, as usual, just after preface. Summarizing, this book offers both a good overview of the main concepts of relative risk estimation and disease, emphasizing insight and intuitive understanding, and practical guidance on how to apply them. The numerous and well laid-out examples encourage the readers to do their own experiments and can be easily adapted to individual needs. This book is designed to be of interest to final-year undergraduate and graduate level statistics and biostatistics students, but will also be of relevance to epidemiologists and public health workers both in higher education and beyond. Because the reader is step by step led into the world of disease mapping, not only experienced researches but any person, even just beginning his own research in the matter, will greatly profit from this book.

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Many books have been written on the medical applications of statistics. Most of them, however, cover the fields of epidemiology, controlled clinical trials or survival analysis. The texts on the statistical evaluation of diagnostic tests are rare, and the book from Margaret Sullivan Pepe is thus welcome.

According to the author, the purpose of the book is to provide a systematic framework for the statistical theory and practice of research studies that seek to evaluate clinical tests used in the practice of medicine. It should serve as both a reference for the statistician applying these techniques in practice and as a survey of the current state of statistical research for the academic interested in developing new methodology in this field. The book is organized in 9 chapters.

Chapter 1 is an introduction to diagnostic and screening tests and to designs used to study their accuracy. The author also presents the common sources of bias and the examples used throughout the book.

Chapter 2 defines the classical measures of accuracy for binary tests, that is, false and true positive fractions (or, equivalently, sensitivity and specificity), positive and negative predictive values and diagnostic likelihood ratios. The chapter also presents the relationship between these parameters, their estimations from a cohort and a case control study, and the metrics used to compare them: absolute differences, odd ratios, and relative probabilities.

The classical approach to comparing binary tests in unpaired and paired designs is provided in chapter 3. This section also presents the regression modeling framework which can be used to identify factors that influence the performance of a test, for comparing tests or for evaluating the incremental predictive value of a test beyond information contained in other sources. The author describes regression models for true and false positive fractions with logit and probit link functions, for predictive values and for diagnostic likelihood ratios.

Chapter 4 presents the concept of receiver operating characteristic (ROC) curve, with its mathematical properties, its alternatives and its main summary indices like the area under the curve (AUC), the ROC (t_0) and partial AUC, the symmetry point and KS index. The author describes the binormal ROC curve and curves for ordinal tests, with the latent decision variable model and the discrete ROC curve. Other parametric models, such as the bigamma model, are not detailed.

In Chapter 5, the author addresses the issue of the estimation of ROC curves. Three approaches are examined. The first one is empirical estimation, a function only of the ranks of the continuous or ordinal test result data. The sampling variability, the confidence intervals, the area under the curve, the KS index and

comparisons between such empirical curves are described. The second approach uses statistical models for the distribution of test results, fully parametric modeling or semi-parametric models. The third approach, called *parametric distribution free*, models the ROC curve rather than the probability distributions as a smooth parametric function. The binormal latent variable framework for ordinal data and the LABROC and ROC-GLM estimates for continuous test results are presented.

Chapter 6 details the methods for studying the covariate effects on continuous and ordinal tests. A first approach models covariate effects on the distribution of test results in the diseased population while the second one directly models the effects on the ROC curve, with the ROC-GLM regression model. The latter specifies how the distribution of results in diseased and non diseased patients are related to each other, in a parametric or semi-parametric way. These approaches parallel the methods used for estimating the curves. The author shows the consequences of omitting covariates and discusses the respective interest of pooled-data ROC curves and covariate-specific ROC curves. The chapter ends by mentioning another approach, modeling of a summary index of a ROC curve as a function of covariates, which is not developed.

Chapter 7 focuses on the problem of incomplete and imperfect reference tests, an often encountered situation in practice. The first form is the verification bias sampling in which subjects are more often sent for definitive diagnosis with the gold standard when study test is positive rather than negative, leading to the use of Begg and Greene's adjusted estimates of true and false positive fractions. A second form occurs when verification is restricted to screen positives, the extreme form of verification bias. The author shows that other measures of accuracy, the detection probability and the false referral probability, can be estimated in this situation, and that diagnostic tests can be compared with regards to the true and false positive fractions, even though the absolute values of these parameters cannot be calculated. A third form of the problem is the imperfect reference test, when a definitive test does not exist. The classical solution of latent class analysis is possible but supposes conditional independence, which implies that, if a subject's true disease status is known, then knowledge of the result of one test is not informative about the result of any of the other tests. Under this assumption, data from at least three tests are required for identifiability of true and false positive fractions of the tests. The author also discusses briefly more complex models, relaxing assumption of conditional independence, but insists that considerable caution should be exercised in using the latent class model approach in practice. The chapter ends by citing two other solutions, the discrepant

analysis which is rightly criticized, and the method of composite reference standard.

Chapter 8 proposes to categorize the development process for a medical test into five distinct phases, adapted from a previous schema of the author for cancer biomarker research. Computing of sample size is detailed for comparing binary and continuous tests in phase 2 and 3 studies, and for inference about false and true positive fractions, predictive values or detection probability and false referral probability in phase 4 studies. The additional strategies of stratification and matching are discussed.

Three additional topics are covered by chapter 9. The author (1) introduces meta-analysis and describes summary ROC curves and binomial regression models; (2) presents methods that acknowledge the time-dependent nature of the disease state and describes time-dependent sensitivity and time-dependent ROC curves; (3) shows how to study the combination of multiple test results, by Boolean combinations or by using likelihood ratio function or risk score function.

Some topics, like reliability and reproducibility, or medical decision making are only mentioned. Others like chance-corrected sensitivity and specificity, three-zone diagnostic tests, spectrum bias, selection of cut-off for continuous tests or the use of information theory for assessing tests, are not covered. I also regret the lack of a historical note, allowing to cite the names of some scientists who have contributed much to this field in the past.

These criticisms are, however, minor with respect to the great quality of the book. The methodology is explained in a correct way and is illustrated through examples from various medical studies, including exercised stress test in coronary artery surgery, biomarkers for pancreatic or prostate cancers, ultrasound for detecting hepatic metastases, ovarian cancer gene expression or neonatal audiology data. The book is well written and easy to read for a biostatistician, but also for a clinician with a sufficient background in statistics. The author has succeeded in reaching a compromise between the mathematical rigour of the academic statistician and the clear teaching of methods in a less technical way for a medical scientist.

In conclusion, I think this book will be very useful to all scientists involved in studies assessing diagnostic tests, and is strongly recommended to both biostatisticians and medical researchers.

Book Review by Faans Steyn (South Africa)

Sylvia Wassertheil-Smoller

Biostatistics and Epidemiology: A Primer to Health and Biomedical Professionals (Third Edition)

Springer (2003) 0-387-40292-6

The author states in the preface of this edition that the book has continued to adapt to evolving areas of research in epidemiology and statistics, while maintaining the original objective of being non-threatening, understandable and accessible to those with limited or no background in mathematics. In my view she had succeed in this objective. Those were also the feelings of some of my academic colleagues in the Health Sciences Faculty of our university. To quote some of their comments: "The book gives a good introduction to basic terminology and statistical methods in layman's language", "All the whys and wherefores during statistical analyses are addressed", "Topics that we use, as hypothesis testing, significance, design of studies, odds ratio, ANOVA and regression are well explained with enough examples" and "One would not be an expert after studying this book, but for people who have not used statistics yet (as our post-graduate students), will well benefit by using this book".

The material of the book is aimed to give an understanding of the underlying principles, as well as practical guidance for application and interpretation. The topics included are those that are commonly used and referred to in the literature of the health and biomedical sciences.

The first chapter on the scientific method deals with the philosophy and logic of science – a topic not frequently encountered in introductory statistical textbooks. I do like this background as an introduction to the underlying framework of the field of statistics and epidemiology.

Since probability theory is a building block of statistics and epidemiology, the second chapter gives a little bit of probability and serves as basis for topics to come. The chapter with heading *Mostly about statistics* deals with the ordinary statistical methods found in introductory textbooks but emphasizing the interpretations along with examples.

The chapter about epidemiology gives a good account of the many rates and ratios in this field. The numerous definitions are well explained in the way of examples and will enable the health science researcher to use the appropriate rates and to interpret them accordingly. The following chapter introduces clinical trials by dwelling also

on topics like "purposes of randomisation" and "how large should a clinical trial be". What I appreciate here is the distinction the author makes between statistical significance and clinical significance.

A chapter about quality of life is added to this edition and deals with topics somewhat unknown to the health scientist: reliability, validity and responsiveness when dealing with scales on questionnaires.

Being a statistical consultant also to researchers in fields other than the health sciences, genetic epidemiology was a new topic to me when reading it in chapter 8. To quote the author: "With the sequencing of human genome, there has been a flowering of research into the genetic basis of health and disease, and especially the interactions between genes and environmental exposures. The medical literature in genetic epidemiology is vastly expanding and some knowledge of the epidemiological designs and an acquaintance with the statistical methods used in such research is necessary in order to be able to appreciate new findings". This chapter is a new addition to former editions of the book and is an unusual feature, since such material is not usually found in a first level epidemiology or statistics textbook.

The last chapter on research ethics and statistics is very relevant for the health science researcher – especially while dealing with experimentation on humans and animals.

As many of the subsections stand alone, the reader can turn to the topic that interests him or her. Also, appendices provide sample calculations for various statistics described in the text. The references of literature for each chapter, together with a list of material for further reading, also give this book a review character.

The audience supposed are (1) physicians doing clinical and basic research; (2) medical, college and graduate students; (3) research staff in various capacities, and lastly; (4) anyone interested in the logic and methodology of biostatistics and epidemiology.

As a statistical consultant I will without hesitation recommend this book to be used by my clients and to readers from the categories above.

Seber and Wild present a book intended to cover a wide range of nonlinear regression topics. In this respect the book can be regarded as a complementary volume to Seber (1977, 1984), which deal with linear regression analysis and multivariate methods. The book consists of 15 Chapters and five appendices. There is a lot of material and many examples provide interesting reading. Each chapter contains examples sampled for each particular theoretical consideration.

The first chapter covers basic definitions and notations as well as various types of models that can be found. This includes the linear and nonlinear models, fixed-regressor model, random-regressor models, controlled regressors with error, generalized linear model, transforming to linearity, models with autocorrelated errors, and further economic models. Chapter 2 describes estimation methods: least squares estimation, maximum likelihood estimation, quasi likelihood estimation, robust estimation, Bayesian estimation, variance heterogeneity. In Chapter 3 some problems are as commonly encountered when fitting nonlinear regression models, are studied. The authors discuss topics associated with the convergence of the iterative methods of computation, the finite application of asymptotic inference theory and ill-conditioning in parameter estimation. Each of these closely interconnected topics are expanded on as they arise in later chapters. In chapter 4, based on intuitive ideas from differential geometry, the previously defined arrays can be used to develop the concepts of intrinsic and parameter-effect curvatures at a point. These curvatures are introduced in section 4.2 along with their interpretation and "reduced" formulae for their computation. They can be useful in assessing the appropriateness of the linear approximation mentioned in this section. Several other curvature measures have also been introduced, and these are discussed briefly in section 4.3; related quantities called statistical curvatures and connection coefficients are introduced in section 4.4. In section 4.5 the curvatures developed in section 4.2 are generalized to deal with subsets from the full parameter set. Finally, several theoretical and empirical methods based on simulation are developed for assessing the effects of nonlinearity on the distributional properties of the least-squares estimate parameters. In Chapter 5 the authors approach asymptotic and exact inferences relating to confidence intervals and regions, and hypothesis testing. The role of curvatures is again

considered, and some aspects of optimal design close the chapter.

Chapter 6 describes autocorrelated errors: AR(1) errors, AR(2) errors, AR(q_1), MA(q_2) errors, ARMA(q_1, q_2) errors, and fitting and diagnosis of error processes. In Chapter 7 and the following chapters the authors make a fairly detailed study of several classes of model that, historically, have provided a good deal of motivation for the statistical development of nonlinear regression. Chapter 7 deals primarily with sigmoidal growth models, though there are sections on the closely related agricultural yield-density models. Chapter 8 discusses compartmental and sums-of-exponentials models. In Chapter 9, change-of-phase models and spline-regression models are considered.

Errors-in-variables models are discussed in detail in Chapter 10 for both explicit and implicit nonlinear models. Multiresponse nonlinear models are considered briefly in Chapter 11. Chapter 12 gives us a glimpse of some of the basic asymptotic theory. Chapters 13 and 14 provide an introduction to the growing literature on algorithms for optimisation and least squares, together with practical advice on the use of such methods in programs. In Chapter 15, software considerations are made for data analysts. Important sources of software for nonlinear optimisation, namely the major subroutine libraries and the Association of Computing Machinery (ACM) algorithms, are given.

The book ends with five appendices, an author index, an extensive list of references, and a subject index. Appendix A deals with matrix results, Appendix B gives an introduction to some basic concepts of differential geometry and curvature, Appendix C outlines some theory of stochastic differential equations, Appendix D summarizes multiple linear regression theory, and Appendix E discusses a minimization subject to linear constraints.

Whilst certain parts of this book are admittedly dated, the majority of the text is highly relevant to every practicing statistician. I hope that Wiley's release of this book, will rekindle some interest in this important and inappropriately overlooked subject.

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Communications iscb-comms@ yahoogroups.com	1. To consider the future of the Newsletter, including ways to support the Editor, procedures for transition of editorship. 2. To maintain the ISCB homepage on the World Wide Web and facilitate placement of annual meeting information on the homepage. 3. To consider other communications with members, such as through email or the World Wide Web.	Chair: David W Warne (CH) Secretary: Bjarne Nielsen (DK) Members: Nancy Geller (USA), Maria Grazia Valsecchi (I), Harry Southworth (UK) John Whitehead (UK)	david_w_warne@bluewin.ch bn@medicon.dk ng@helix.nih.gov grazia.valsecchi@unimib.it harry_southworth@yahoo.co.uk j.r.whitehead@reading.ac.uk
Conference Organising iscb-conf-org@ yahoogroups.com	1. Bring together ISCB conference organisers or ISCB members who have an interest in sharing and passing on their knowledge and experience to help future ISCB conference organisers. 2. Document processes and systems for assisting ISCB conference organisers. 3. Review and update the documents whenever necessary and promote their usage for improving the procedures or meetings.	Chair/Secretary: Harbajan Chadha-Boreham (CH) Members: Elia Biganzoli (I) Emmanuel Lesaffre (B) Bjarne Nielsen (DK) Catherine Quantin (F) Norbert Victor (D) John Whitehead (UK) Koos Zwinderman (NL) David W Warne (CH) Giota Touloumi (GR)	Harbajan.Chadha-Boreham@Actelion.Com biganzoli@istitutotumori.mi.it emmanuel.lesaffre@med.kuleuven.ac.be bn@medicon.dk catherine.quantin@chu-dijon.fr victor@imbi.uni-heidelberg.de j.r.whitehead@reading.ac.uk a.h.zwinderman@amc.uva.nl david_w_warne@bluewin.ch gtouloumi@med.uoa.gr
Dentistry iscb-dentist@ yahoogroups.com	The aims are to: 1. Bring together statisticians who have a major interest in dental statistics 2. Review the statistical quality of the current dental clinical trials 3. Promote education and research on statistical methods in dentistry 4. Contribute to statistical issues in regulatory guidelines	Chair/Secretary: Emmanuel Lesaffre (B) Members: Carol Redmond (USA), Ian Needleman (UK), David Moles (UK) Maria-Jose Garcia-Zattera (B) Heidi Huber (USA)	emmanuel.Lesaffre@med.kuleuven.ac.be ckr3@pitt.edu I.Needleman@eastman.ucl.ac.uk d.moles@eastman.ucl.ac.uk MariaJose.GarciaZattera@med.kuleuven.be hmrch@pitt.edu
Education iscb-education@ yahoogroups.com	To organise one or two day courses on contemporary methods in clinical biostatistics which will involve one or several members as lecturers which will be presented in locations represented by the Society. Guidelines and plans of previous courses are available.	Chair/Secretary: Rumana Omar (UK) Members: Mike Campbell (UK), Nicole Close (USA), Carol Redmond (USA), Maria Grazia Valsecchi (I), Havi Murad (ISR), Elisabeth Svensson (S), Catherine Quantin (F) Jeno Reiczigel (H) Eric Cobo (E)	Rumana@stats.ucl.ac.uk m.j.campbell@sheffield.ac.uk nclose@emmes.com ckr3@pitt.edu grazia.valsecchi@unimib.it havim@gertner.health.gov.il elisabeth.svensson@esi.oru.se catherine.quantin@chu-dijon.fr jreiczig@univet.hu erik.cobo@upc.edu

How to Contact the ISCB Subcommittees (continued)

Title & Email	Terms of Reference	Members	Email addresses
Membership	To explore strategies to increase the ISCB membership by means of: 1. Highlighting the unique position of the ISCB, i.e. bringing together clinicians, methodologists, epidemiologists and biostatisticians 2. Make strategic links with medical and epidemiological societies in order to make publicity at their meetings and bring clinicians/epidemiologists with a methodological/biostatistical interest to our ISCB meeting 3. Widen the geographical spread of the ISCB members 4. Ensure the regeneration of our current core membership. 5. Provide guidelines for future conference organisers on choosing a scientific programme committee that will help in widening membership	Chair/Secretary: Emmanuel Lesaffre (B) Members: Harbajan Chadha-Boreham (CH) Norbert Victor (D), John Whitehead (UK)	emmanuel.Lesaffre@med.kuleuven.ac.be Harbajan.Chadha-Boreham@Actelion.Com victor@imbi.uni-heidelberg.de j.r.whitehead@reading.ac.uk
National Groups Isccb-national-groups@yahoo.com	1. To help those who are interested in forming a National Group through the approval process. 2. To review the arrangements with the current National Groups, specifically regarding financial matters. 3. To set rules and standards for funding of ISCB members of National Groups and others from countries with exchange control restrictions or barriers. 4. The Subcommittee administers the Conference Awards for Scientists for the annual ISCB meetings.	Chair/Secretary: Michael Schemper (A) Members: Elia Biganzoli (I), Krista Fischer (EST) Ewa Kawalec (PL), Catherine Quantin (F) Julia Singer (B), Norbert Victor (D), John Whitehead (UK)	Michael.schemper@meduniwien.ac.at biganzoli@istitutotumori.mi.it Krista.Fischer@ut.ee mxkawale@cyf-kr.edu.pl catherine.quantin@chudijon.fr JSINGER2@PRDBE.JNJ.COM victor@imbi.uni-heidelberg.de j.r.whitehead@reading.ac.uk
Statistics in Regulatory Affairs isccb-reg-aff@yahoo.com	The subcommittee on Regulatory Affairs will review, comment upon and seek to influence the development of regulatory requirements, guidelines and other documents concerning the scientific aspects of data generation, collection, management, analysis, and reporting. In general, the subcommittee will seek out and handle all regulatory issues in the name of the Society with the approval of the President or in his/her absence, the Vice-President.	Chair: Jørgen Seldrup (F) Secretary: Stephen Senn (UK), Members: Helmut Schäfer (D), Harbajan Chadha-Boreham (CH), Anna Petroccione (I) Martin Schumacher	Jorgen.seldrup@quintiles.com Stephen@stats.gla.ac.uk hsimbe@med.uni-marburg.de Harbajan.Chadha-Boreham@Actelion.Com anna.petroccione@nervianoms.com ms@imbi.uni-freiburg.de
Student Conference Awards isccb-stud-conf-awrd@yahoo.com	Student conference awards are available for registered postgraduate students to attend the annual meeting and present a paper. The Subcommittee shall receive submissions, judge them, and administer the awards. The rules are announced in a timely issue of the Newsletter.	Chair/Secretary: Marie Reilly (S) Members: Marc Buyse (B), Bruno Cesana (I), Jan Lanke (S), Vana Sypsa (GR) KyungMann Kim (USA)	Marie.Reilly@ki.se Marc.Buyse@iddi.com cesana@med.unibs.it jan.lanke@stat.lu.se vsipsa@cc.uoa.gr kmkim@biostat.wisc.edu

ISCB Membership Information

The **International Society for Clinical Biostatistics (ISCB)** was founded in 1978 to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine.

The ISCB organises an annual scientific meeting which members and non-members are able to attend. The main objective of the annual scientific meetings is to create an opportunity for the exchange of knowledge, experience and ideas among clinicians, statisticians and members of other disciplines, such as epidemiologists, clinical chemists and clinical pharmacologists, working or interested in, the field of clinical biostatistics.

The scientific meetings cover a broad spectrum of biostatistical interests and regularly include sessions on the design and analysis of clinical trials, epidemiology and statistical methodology, as well as from time to time considering more specialist issues such as, for example, education of biometricians and biometrics users, pharmacokinetics, medical data-bases and pharmaco-epidemiology.

Meetings in recent years have been held in Stockholm (2001), Dijon (2002), London (2003), Leiden (2004) and Szeged (2005) and the next meeting will be held in Geneva (2006). A selection of talks at the meetings, for which papers are submitted for review and which are eventually accepted, are published in *Statistics in Medicine*. The ISCB benefits from a special journal concession from John Wiley & Sons Limited, the publishers of *Statistics in Medicine*, so that members are able to subscribe to the journal at a preferential rate.

The ISCB also organises courses to cover particular statistical topics. These are run to precede or follow on from the annual scientific meeting and are given by the foremost researchers in the field.



The composition of the **Executive Committee** (ExCom) for 2006 is as follows:

Officers:

President: John Whitehead (UK),
Vice-President: Emmanuel Lesaffre (B),
Secretary: Harbajan Chadha-Boreham (CH),
Treasurer: Norbert Victor (D).

Members:

News Editor: David W. Warne (CH),
Webmaster: Bjarne Nielsen (DK),
Past-President: Maria Grazia Valsecchi (I),

Peter Lachenbruch (USA), Rumana Omar (UK), Catherine Quantin (F), Jeno Reiczigel (H), Marie Reilly (S), Martin Schumacher (D), Vana Sypsa (GR), Koos Zwinderman (NL).

The Annual General Meeting of the ISCB is organised to coincide with the scientific meeting. Membership of the Society is drawn from about 40 countries worldwide and the number of members is nearly 800.



The ISCB also has special **Subcommittees** dealing with particular aspects of biostatistics.



The Society publishes a **Newsletter** twice a year. The ISCB News editor is David W. Warne, Chemin du Petit-Bel-Air 115, CH-1226 Thônex, Switzerland. Items for inclusion in the Newsletter should be sent to him via email to: **david_w_warne@bluewin.ch**


Membership of the Society is open to all with an interest in biostatistics. The current annual (to 31 December 2006) Ordinary membership fee is €40. The Full-time Student Membership fee is €20.

Applications for membership should be sent to:

ISCB Permanent Office,
P.O. Box 130,
Datavej 24,
DK-3460 Birkerød, Denmark

Tel. +45 4567 2279
Fax +45 7022 1571
email: office@iscb.info
www: <http://www.iscb.info>

**INTERNATIONAL SOCIETY FOR CLINICAL BIOSTATISTICS
2006 Membership Subscription**

Surname: _____		First Name: _____	
Title (Prof/Dr/etc): _____		Post held: _____	
Address: _____ _____			
Post code and country: _____			
Phone No: _____		Email: _____	
Fax No: _____		Please provide your email address as it will be used to send you the ISCB News in the future.	
SUBSCRIPTION:			
<input type="checkbox"/> Ordinary membership of ISCB (to 31 December 2006):		Euros (EUR) 40.00	
(please tick only one) <input type="checkbox"/> Full-time Student Membership of ISCB (to 31 December 2006):		Euros (EUR) 20.00	
(students should provide a letter from their supervisor or head of department)			
Have you previously been a member of ISCB? ?Yes ?No			
PAYMENT IS MADE BY:			
Credit Card Authorisation: ?VISA ?VISA Electron ?Master Card ?Euro Card ?JCB			
Signature: _____		Date: _____	
Your name on credit card: _____		Card number to debit (16 digits): _____	
		Validation code (3 digits) (CVC/CVV) _____ from the back of your credit card	
_____		_____	
Cheque/Money Order:			
<input type="checkbox"/> A cheque made payable in Euros - drawn on a bank in the United Kingdom			
<input type="checkbox"/> A Money Order			
Cheque / Money Order No: (if known) _____		Date sent: _____	
Cheques must be made payable to the International Society for Clinical Biostatistics and returned with this form to the Permanent Office address.			
Note: Non -Euro cheques, bank cheques not drawn on a U.K. bank, and cheques not made payable to ISCB will be returned.			
Bank Transfer:		<input type="checkbox"/>	
Please transfer direct to:		Euro Account No. 6687 4511	
Barclays Bank plc		Bank Sort Code: 20-18-15	
PO Box 69		IBAN: GB28 BARC 2018 1566 8745 11	
121 Queen Street		SWIFT/BIC: BARCGB22	
Cardiff CF1 1SG			
UK			
Please return this form either by Email to:		office@iscb.info	
or by post to:		ISCB Permanent Office P.O. Box 130 Datavej 24 DK-3460 Birkerod Denmark	
Tel: +45 4567 2279			
Fax: +45 7022 1571			
			

Calendar

27-31 August 2006

Geneva, Switzerland

ISCB27

Info: David W Warne email: david_w_warne@bluewin.ch, web: <http://www.iscb2006.info>

29 July - 02 August 2007

Alexandroupolis, Greece

ISCB28

Info: Giota Touloumi email: gtouloum@med.uoa.gr, hotel web: <http://www.thrakipalace.gr>



For the latest conference info, see:

<http://isi.cbs.nl/calendar.htm>



Mar 14 - 17	Frankfurter Stochastik-Tage / German Open Conference on Probability and Statistics. This conference is held every two years by the Fachgruppe Stochastik of the German Mathematical Society. It provides a forum for participants from universities, business, and industry to discuss new results in the area of probability and statistics. To be held at the "Campus Westend" of Goethe University, Frankfurt am Main, Germany. Information: Anton Wakolbinger (Chairman of the Program Committee) Phone: +49 798 28651 or +49 798 23722 Fax: +49 798 28444 E-mail: wakolbinger@math.uni-frankfurt.de Website: http://stoch2006.math.uni-frankfurt.de/index_en.html	Jun 11 - 15	21 st Nordic Conference on Mathematical Statistics (NORDSTAT) is a biennial meeting for statisticians and probabilists from the countries in Northern Europe. NORDSTAT also welcomes participants from countries outside Scandinavia. Website: http://www.dsts.dk/nordstat2006/index.html	Jul 24 - 28	The 17 th Brazilian Symposium of Probability and Statistics, will be held at the Hotel Gloria, in the city of Caxambu, Minas Gerais state. The program includes conferences, short courses, round tables, oral and poster communications. Information: Associação Brasileira de Estatística C. P. 66281 - Ag. Cidade de São Paulo 05315-970 São Paulo - SP Brasil E-mail: abe@ime.usp.br Website: http://www.redeabe.org.br
Mar 20 - 24	Conference on Stochastics in Science. In Honor of Ole E. Barndorff-Nielsen's 71 st birthday. CIMAT, Guanajuato, Mexico. E-mail: pabreu@cimat.mx Website: www.cimat.mx/Eventos/oebn-conference	Jul 2 - 7	ICOTS-7: <i>Working Cooperatively in Statistics Education</i> , Seventh International Conference on Teaching Statistics, to be held at the Othon Hotel in Salvador, Bahia, Brazil. The major aim of ICOTS-7 is to provide the opportunity for people from around the world to exchange ideas and experiences in teaching statistics and to expand their network of statistical educators Information: Carmen Batanero Phone: +34-958-243950 Fax: +34-958-246359 E-mail: batanero@ugr.es Website: http://www.maths.otago.ac.nz/icots7 , http://Auga.otago.ac.nz/icots7/icots7.php	Aug 6 - 10	Joint Statistical Meeting, organized by the American Statistical Association and to be held at the Seattle Convention Center, Seattle, Washington. Website: www.amstat.org/meetings
Apr 19 - 21	Second International Meeting <i>Methodological Issues in Oral Health Research: Assessing and Improving Data Quality</i> , to be held in Het Pand, a medieval abbey in Ghent, Belgium. This international meeting aims to bring together oral health researchers and statisticians interested in the analysis of dental data. The ultimate goal is to stimulate collaboration between the two parties eventually leading to the improvement of the methodological quality of oral health papers and the stimulation of new statistical research useful for the analysis of dental data. Website: http://med.kuleuven.be/biostat/conferences/Dental2006/	Jul 2 - 7	The combined Australian Statistical Conference / New Zealand Statistical Association Conference 2006 (ASC/NZSA) will be held at the SkyCity Hotel in Auckland, New Zealand. Areas of statistics include: medical, financial, environmental and social statistics, statistical computing, data mining and bio-Informatics. Phone: +61-292650700 E-mail: statsnz2006@tourhosts.com.au Website: www.statsnz2006.com	Aug 23 - 25	Workshop on Data and Information Visualization, to be held at the Humboldt-Universität zu Berlin, Wirtschaftswissenschaftliche Fakultät, Berlin, Germany. See Compstat 2006
May 17 - 19	CASI 2006: Conference of Applied Statistics in Ireland Cork, Ireland. Deadline for submissions: 28 th Feb 2006. Invited Speakers: David Brillinger, John Crowley, David Giltinan, Grace Wahba. Location: Hotel Europe, Killarney, Ireland Information: Kingshuk Roy Choudhury, Statistics Department, University College Cork, Ireland. E-mail: kingshuk@stat.ucc.ie Website: http://euclid.ucc.ie/pages/casi06/index.html	Jul 2 - 7	The 21 st International Workshop on Statistical Modelling (IWSM 2006) to be held at the National University of Ireland, Galway. This annual meeting of the Statistical Modelling Society is devoted to all aspects of statistical modelling and includes invited and contributed sessions and a pre-conference short course. Information: John Hinde Phone: +353 91 492043 Fax: +353 91 494542 E-mail: john.hinde@nuigalway.ie Website: http://www.nuigalway.ie/math/IWSM2006	Aug 28 - Sep 1	COMPSTAT 2006: The 17 th Conference of the International Association for Statistical Computing (IASC) will be held in Rome, Italy. Satellite meetings: KNEMO , Data and Information Visualization , Statistical Latent Variables Models E-mail: compstat2006@uniroma1.it Website: http://w3.uniroma1.it/compstat2006
May 28 - 31	SSC-2006: Annual Meeting of the Statistical Society of Canada, London, Ontario. The University of Western Ontario will be hosting the 2006 meeting of the Statistical Society of Canada. Information: Local Arrangements Chair: David Bellhouse Phone: (519) 661-3614 Fax: (519) 661-3813 E-mail: bellhouse@stats.uwo.ca	Jul 16 - 21	XXIII rd International Biometric Conference to be held in Montreal, Quebec, Canada. Website: http://www.ibt2006.org	Sep 10 - 14	Royal Statistical Society 2006 International Conference, Queen's University, Belfast, U.K. Key topics will include: official (regional) statistics, machine learning, environment/climate change, communication of statistics, medical statistics/bioinformatics, statistics and the law. Information: Paul Gentry Phone: +44 (0)20 7614 3918 Fax: +44 (0)20 7614 3905 E-mail: conference@rss.org.uk Website: www.rss.org.uk/rss2006
Jun 5 - 9	PROBASTAT 2006, 5 th International Conference on Probability and Statistics, to be held at Smolenice Castle, Slovak Republic. Information: Dr. Viktor Witkovsky, Institute of Measurement Science, Slovak Academy of Sciences, Dubravská cesta 9, 84104 Bratislava, Slovakia E-mail: probastat@savba.sk Website: http://aiolos.um.savba.sk/~viktor/probastat.html	Jul 16 - 21	International Conference on Robust Statistics (ICORS 2006), Technical University of Lisbon, Portugal. ICORS is the main meeting devoted to discuss recent results and to present the state-of-the-art on robust statistics and related subjects. The conference will include invited lectures, contributed papers and poster sessions. Both theoretical and applied contributions are welcome. Fax: +351-218417048 E-mail: icors2006@math.ist.utl.pt Website: http://www.math.ist.utl.pt/icors2006	Nov 1 - 3	Ottawa, Canada The 23 rd International Methodology Symposium "Methodological Issues in Measuring Population Health", organised by Statistics Canada, will bring together statistical methodologists and analysts addressing a variety of topics related to producing reliable information on population health. Information: Joanne Moloney Phone: 613-951-1469 E-mail: symposium2006@statcan.ca or joanne.moloney@statcan.ca
		Jul 24 - 28	26 th European Meeting of Statisticians, Thorun, Poland. Information: Adam Jakubowski (Chairman of the Local Organising Committee) Website: www-m4.mathe.matik.tu-muenchen.de/m4/erc/ , http://www.ems2006.umk.pl		