

International Society for Clinical Biostatistics

News

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Correspondence Address

David W. Warne **ISCB News Editor**
 Home: Chemin du Petit-Bel-Air 115,
 CH-1226 Thônex, Switzerland.
 Tel: +41 22 700 6380
david_w_warne@bluewin.ch
 Work: Tel: +41 22 739 3374,
 Fax: +41 22 739 3330

Editorial

There are just a few weeks to go until the Society's 26th conference in Szeged, Hungary. This is the Society's visit to the east of Europe and it promises to be as good a meeting as the previous Hungarian conference in 1996. From a quick look at the draft programme, there's a wide range of topics and speakers from 20 countries.

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, and the Szeged LOC/SPC for providing the draft conference programme.

Financial News

From the Treasurer & Permanent Office

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www: <http://www.iscb.info>
 Permanent Office: office@iscb.info
 Book review Editor: harry_southworth@yahoo.co.uk

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ISCB Membership

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		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	Jun 05
*=host of	conference															
	Total	261	596	715	698	725	702	685	729	818	797	837	825	756	758	436
	# Countries	23	32	32	31	33	34	37	37	41	40	45	41	40	38	33
1.	UK	50	90	176*	120	144	121	128	169*	135	151	153	141	190*	140	65
2.	Germany	30	67	75	84	71	78	72	70	186*	90	87	77	61	57	42
3.	Poland [NatGrp]		11	11	24	24	30	21	19	26	34	37	41	41	43	40
4.	USA	18	45	40	39	41	40	79*	66	76	77	89	78	75	57	38
5.	Hungary [NatGrp]	1	21	17	18	19	25*	27	29	29	33	34	41	48	42	38*
6.	Romania [NatGrp]						2			4	1	1	1	19	21	30
7.	Denmark	4	58*	38	31	30	32	26	35	38	39	36	46	41	37	22
8.	Netherlands	14*	30	38	33	36	29	31	39	35	33	38	39	33	87	21
9.	Sweden	23	51	53	54	58	64	51	45	38	44	88*	50	36	34	19
10.	France	30	52	62	50	73	67	52	52	49	53	37	93*	31	41	17
11.	Switzerland	14	25	22	80*	33	29	24	25	23	18	23	26	22	23	16
12.	Belgium	13	22	27	30	30	32	35	29	25	33	36	33	23	27	16
13.	Italy	16	33	37	32	32	33	26	33	26	63*	29	25	15	25	11
14.	Norway	13	18	25	22	12	18	10	10	11	10	16	16	12	14	10
15.	Japan	2	6	7	5	7	4	10	13	20	12	11	10	10	10	6
16.	Canada	6	12	14	14	11	13	15	14	9	9	10	14	16	8	6
17.	Austria	4	9	11	13	11	16	13	11	15	18	15	13	16	17	5
18.	Finland	2	7	7	9	9	9	7	5	10	9	18	11	7	11	5
19.	Australia	6	9	11	6	9	8	11	9	10	12	8	9	14	8	5
20.	Spain	10	12	18	12	46*	23	14	16	12	11	11	8	7	15	3
21.	Slovenia		1	2	3	2	1	1	3	2	1	2	1	2	3	3
22.	Malaysia					2	1	2	2	1	1	1	1	1	3	3
23.	India		1	1	1	1	1	1	1	1	2	1	2	2	3	2
24.	Singapore							3	6	4	5	8	5	7	2	2
25.	South Africa		1	4	1	3	2	2	2	2	2	3	3	3	2	2
26.	Czech. Rep.			1	1	1	1	1	1	2	2	1	1	1	1	2
27.	Israel	1	3	4	4	4	4	3	3	4	10	13	10	7	8	1
28.	Russia					1	3	3	3	2	2	1	4	3	2	1
29.	Mexico						1	1	1	1	1	1	2	2	2	1
30.	Greece		1	1	1				1	1	3	1	6	1	2	1
31.	Turkey		1	1						1				1	2	1
32.	New Zealand		1		1		2	1	2	2	2	3	3	3	1	1
33.	Taiwan										1	1	1	1	1	1
34.	Iran						1	1					1	1	4	
35.	Cuba								2	2	2	2	2		2	
36.	Portugal	1	3	5	2	2	2	2	5	5	3	4	3	3	1	
37.	Malawi												1	1	1	
38.	Ireland	1	2	3	4	3	4	4	2	3	2	3		1	1	
39.	South Korea					3		1						1		
40.	Estonia											2		1		
41.	Colombia							1	1		1			1		
42.	China		1	1	2	3	3	3	3	3	3	3	2			
43.	Thailand		1	1		1	1	2	1	1	2	2	2			
44.	Croatia									1	1		1			
45.	Gambia												1			
46.	Slovakia												1			
47.	Lithuania											2				
48.	Argentina											1				
49.	Brazil					2						1				
50.	Kuwait	1										1				
51.	Saudi Arabia											1				
52.	Sudan											1				
53.	Ukraine									1		1				
54.	Egypt											1				
55.	Pakistan								1	1	1					
56.	Philippines									1						
57.	Indonesia						1									
58.	Zimbabwe				1											
59.	Kenya		1	1												
60.	Oman	1														

President's Mid-Year Message

From John Whitehead

As our Annual Scientific Meeting in Szeged approaches, I am hearing positive reports about the number of abstracts received. The precise relationship between the number of abstracts submitted and the number of participants eventually registered at ISCB conferences has never been formally statistically analysed, but I think that we can be confident of a good turn-out. If you have not registered already, I hope that you will. Not only have the Scientific Programme Committee organised an excellent programme, but the Local Organising Committee are arranging a warm welcome for us all.

The ISCB has a faithful core membership, dedicated to following the Society's progress around the cities of Europe, and occasionally beyond. I look forward to seeing you all again this year. The Society relies on you, not just to participate yourself, but to introduce new and younger members to our activities. One theme of the discussions of the Executive Committee this year will be how to expand our membership to greater numbers and to people with a wider range of interests. Suggestions will be welcomed by Committee Members and at the AGM.

The Executive Committee has been refreshed this year with an intake of newly elected members. We are grateful to them for agreeing to serve, and to those members who participated in the ballot. The Society's Permanent Office is now firmly re-established in Denmark and operating smoothly. The efforts of Rita Schou in running our affairs so capably should not go unremarked.

Although the Society has only one meeting each year, there are always several under consideration at any one time. The Society's Officers have recently received the final accounts from Leiden, and only now is the work of the organisers of that successful meeting complete. A great amount of preparatory work is going on for the Geneva meeting in 2006, and some of the plans will be presented at this year's AGM. Two other groups are beginning their investigations for hosting us in 2007 and 2008. Should any groups be nursing a plan to invite us all for 2009, please let us know sometime this year.

ISCB26 Szeged 2005: AGM Agenda

From Harbajan Chadha-Boreham

The Annual General Meeting (AGM) will be held in the "Auditorium" at the conference site on Tuesday 23 August 2004, from 1200 to 1300. The agenda is the following:

1. President's report
2. Treasurer's report
3. Subcommittee reports and motions for continuation:

Statistics in Regulatory Affairs,
Education,
National Groups,
Communications,
Student Conference Awards,
Statistics in Dentistry,
Conference Organising

4. Future ISCB meetings: 2006 Geneva (CH)
5. Any other business

ALL participants of the Szeged meeting, even newcomers to ISCB are, by definition, full ISCB members and are, therefore, most welcome to attend the AGM. Please take part!

ISCB26 Szeged 2005: Student Conference Awards: Winners

From Marie Reilly

The three winning papers from this year's SCA competition are:

- **Holly Janes**, University of Washington, USA
"Adjusting for Covariate Effects in Biomarker Studies Using the Subject-Specific Threshold ROC Curve"

- **Katherine Lee**, Cambridge University, UK
"Robust parametric models for random effects"
- **Spyridoula Tsonaka**, Catholic University Leuven, Belgium
"Power and sample size calculations for discrete bounded outcome sources"

ISCB26 Szeged 2005: Conference Awards for Scientists: Winners

From Michael Schemper

A total of 12 applications for the *Conference Awards for Scientists* for ISCB26 in Szeged, Hungary, were received and according to a judgement by the National Groups Subcommittee the following 8 award winners were selected:

Urszula Biela (Poland): Relationship between overweight with high waist to hip ratio and demographic, socioeconomic factors and smoking in middle aged residents of Kraków.
Cornelia Enachescu (Romania): Statistical methods for osteoporosis risk estimation. Application to a clinical study.
Maria Fazekas (Hungary): Analysing Hungarian mortality rates and acute childhood lymphoid leukaemia.
Anneke Grobler (South Africa): Sample size calculations for a clinical trial with more than two arms
It is anticipated that at least 6 awards can be granted for the ISCB meeting in Geneva, 2006.

using a common control group assessing time-to-event. An overview of available methods and a proposed stopping rule.

Piotr Jurkowski (Poland): Assessment charts of constituent and combined classifiers performance for asthma and schizophrenia diagnosis.
Stanislav Katina (Slovakia): Regression partitioning and statistical shape analysis in prediction of sagittal intermaxillary relations in patients with complete unilateral cleft lip and palate during puberty.
Norbert Solymosi (Hungary): Finding spatial barriers by Monmonier's algorithm.
Corina Vernic (Romania): Multivariate analysis of the factors involved in smoking and drinking in an adolescent population.

Book Review by Victor Moreno (Spain)

Richard M Simon, Edward L Korn, Lisa M McShane, Michael D Radmacher, George W Wright, Yingdong Zhao

Design and Analysis of DNA
Microarray Investigations

Springer [2004]
0-387-00135-2

This relatively short book fills a gap in the emerging literature on microarray data analysis. It is written in simple language and the organization of the topics helps the reader easily gaining insight into this field from a description of the technology to the statistical procedures for analysis available. The book is oriented to a multidisciplinary reader, suitable both for researchers with statistical background aiming to understand the basis of the technology and the tricks of the experiments and the researcher with more biological background aiming to understand the statistical methods of design and analysis. Most of the techniques described differentiate whether the microarrays are two channel (two-colour cDNA microarrays) or single channel (Affymetrix GeneChip™ oligonucleotide microarrays). Throughout the book, the methods explained are shown using 6 real datasets from published investigations that are publicly available. These are explained in an appendix with information so that the reader can get the original data. The authors encourage analyzing these datasets with any software the reader may use, and offer, for those without any, a suite of tools called BRB-ArrayTools implemented as an add-in for Microsoft Excel.

Obviously, the authors of this short book do not try to exhaustively cover all the methods used to analyse microarray data, but have made an effort to select those that have consolidated as useful during the last years. They make a clear distinction between 3 groups of techniques: class comparison, class prediction and class discovery. In a few pages, the most relevant aspects of the microarray technology are explained (chapter 2). This chapter is complemented with one appendix on basic biology of gene expression, useful for those with little biological background. Regarding experimental design (chapter 3), emphasis is done in distinguishing biological replicate from technical replicate and the number of replicates needed. The possibility of sample pooling is commented and there is nice discussion about design alternatives for sample comparison using 2-channel arrays: the reference design, the balanced block design and the loop design. About image analysis (chapter 4), the importance of background correction is stressed. Quality controls of data before analysis (chapter 5) are emphasized. Methods for detection of suspicious wrong spots are commented based on size, signal level signal/background ratio and use of duplicate spots. Also quality criteria to assess whole array hybridisation are mentioned. The chapter ends with some methods for data imputation to use for analysis with multiple genes. Data normalization is presented as an essential procedure before comparisons of data between arrays can be done (chapter 6). The choice of genes to use for the normalization procedures and the basic methods for 2-color arrays and for single-channel arrays are shown. After these chapters on design and preliminary data preparation, the last 3 are devoted to statistical procedures of analysis stressing the importance of the aim of the analysis: class comparison, prediction or discovery.

Class comparison (chapter 7) aims to identify genes that are differentially expressed between pre-specified classes. Methods for this range from the basic Student's t-Test for 2 classes or F-statistic for more than 2, to the non-parametric and permutation-based versions of these. Methods for controlling for multiple comparisons are also discussed here: form Bonferroni to multivariate permutation methods and those to control the false discovery rate. Finally the chapter presents modelling methods of analysis, including those to study survival to discover genes associated to prognosis.

Class prediction research (chapter 8) aims to develop a multivariate model that accurately predicts class membership (phenotype) of a new individual (specimen). Similarly to class comparison, class prediction requires that each individual real class is known in order to develop the prediction model. As a first step, the authors propose methods to select the set of genes from which to develop the prediction model (feature selection). Then a series of standard methods to develop class predictors are briefly discussed: discriminant analysis and its variants, nearest neighbours, trees and support vector machines. Finally methods to estimate the error rate of the predictor and a nice example are presented.

Class discovery (chapter 9) aims to identify groups of co-expressed genes or finding patterns in expression profiles of different specimens when there is no predefined class variable to supervise the analysis. The authors propose to start with the choice of a similarity or distance measure, then to display graphically the data using data reduction techniques like multidimensional scaling to gain insight about potential groups and finally addressing formally the class discovery problem with the choice from a set of clustering methods available, mainly hierarchical, k-means or self-organizing maps. Methods for assessing the validity of the clusters are also discussed.

In conclusion, this book is an excellent starting point for both biologists and statisticians aiming to do research using microarray data. The strongest value is the effort made to select those consolidated techniques that makes the book short and easy to read and to avoid mentioning the myriad of variants of methods that appear everyday in the literature with questionable improvement about the standards.

Advertisement: Oxford

Assessing Quality of Life in Clinical Trials

OXFORD
UNIVERSITY PRESS

Second Edition

Edited by Peter Fayers
and Ron Hays



Researchers in all clinical fields are fully aware of the importance of Quality of Life measurements in judging the efficacy of a given treatment. This book explores the current state of the art in the field and illustrates the benefits and potential of health related quality of life assessment in clinical trials. It covers a wide range of analytical issues, emphasizing new and innovative approaches that are of practical and clinical importance.

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MARCH 2005 / 464 PP

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Book Review by Friederike Barthel (UK)

Shein-Chung Chow & Jen-Pui Liu	Design and Analysis of Clinical Trials: Concepts and Methodologies (2 nd ed.)	John Wiley [2003] 0-471-24985-8
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Chow & Liu provide a concise and comprehensive reference book for all parties concerned in the conduct of a clinical trial. They assume only a limited mathematical and statistical background. This second edition of the book first published in 1998 differs from the first edition in three main ways. Firstly, sections have been updated and/or revised to reflect good clinical practice in the regulatory review and approval process as well as recent developments in the design and analysis of clinical research. In part, this has been necessitated by the ICH (International Conference on Harmonization) guidelines. Secondly, three new chapters and new topics have been added which include "Designs for Cancer Clinical Trials" (Chapter 6), "Preparation and Implementation of a Clinical Protocol" (Chapter 14) and "Clinical Data Management" (Chapter 15). Finally, this second edition includes more than 280 new references from clinical-related literature.

Chapter 1 introduces the reader to the topic of clinical trials and answers questions on the definition of a clinical trial, the regulatory process as well as the required contents of the trial protocol. In addition, this chapter includes the aims and structure of the book.

The remainder of the book is split into three main parts. Chapters 2 to 7 cover the concepts of design and analysis of clinical trials. Methodologies and various issues, which are commonly encountered in the analysis of clinical data, are explored in Chapters 8 to 13. The last part of the book covers issues of study protocols and clinical data management in Chapters 14 and 15.

Since the book has been written for readers with minimal mathematical and statistical background knowledge basic statistical concepts such as uncertainty, bias, variability, confounding,

interaction, clinical significance and equivalence, and reproducibility are introduced in Chapter 2. However, in order to take full advantage of the remainder of the book an introductory statistics course may be helpful.

Chapter 3 provides some fundamental considerations for choosing a valid and suitable design for achieving study objectives of clinical trials under various circumstances. Furthermore, as an addition to the first edition, goals of clinical trials and the target population are examined.

Chapter 4 illustrates the concepts and different methods of randomisation and blinding, which are critically indispensable for the success and integrity of clinical trials. Chapter 5 introduces different types of statistical designs for trials and discusses their merits and disadvantages. Designs described here include parallel group, cross-over, titration, enrichment, clustered, group-sequential, placebo-challenging, and blind-reader studies.

As mentioned above, Chapter 6 is devoted to cancer clinical trials. These designs include standard escalation, accelerated titration, and the continual reassessment method (CRM) in determination of the maximum tolerable dose (MTD) for phase I cancer trials. Simon's optimal two-stage design and randomised phase II designs are also discussed.

Further types of clinical trials are discussed in Chapter 7. These include multi-centre, superiority, dose-response, active control, drug-to-drug interaction, combination, and bridging trials. In addition to the material covered in the first edition of the book equivalence and non-inferiority trials as well as vaccine clinical trials are introduced.

Chapters 8, 9 and 10 discuss the advantages and limitations of statistical methods for the analysis of continuous,

categorical and censored data. Group sequential procedures for interim analyses are also introduced in Chapter 10.

Chapter 11 provides different procedures for sample size calculation for various types of data under different study designs. Chapter 12 discusses statistical issues in analysing efficacy data. These include baseline comparisons, intention-to-treat analysis versus per-protocol analysis, adjustment of covariates, multiplicity, the use of genomic information for the assessment of efficacy, and data monitoring.

Chapter 13 focuses on the issues of the analysis of safety data, which include the extent of exposure, coding and analysis of adverse events, the analysis of laboratory data, and the use of genomic information for the evaluation of drug safety.

The structure and components of an adequate and well-controlled clinical trial protocol, issues which are commonly encountered in protocol development, commonly experienced deviations in the conduct of a clinical trial, monitoring, regulatory audit and inspection, and assessment of the quality and integrity of clinical trials are discussed in Chapter 14. Chapter 15 summarizes basic standard operating procedures for good clinical data management practice.

This book's appeal lies in its comprehensive coverage of the subject as well as the easy readability. The authors have provided real examples from clinical trials, which aid the understanding of clinical and statistical concepts and interpretations and provide for interesting reading. In particular, this book is suitable for physicians and scientists as well as clinical researchers. It may also serve as an introductory text for biostatisticians or as a textbook for graduate courses.

Book Review by Harry Southworth (UK)

Peter J. Rousseeuw and Annick M. Leroy	Robust Regression and Outlier Detection	Wiley (2004) 0-471-48855-0
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A member of the Wiley Interscience range, this book was originally released in hardback in 1987. The hardback edition is still available and costs more than double this edition. As such, this version, whilst not a giveaway, offers the opportunity to make a significant saving over the only available version heretofore. I also noticed, in browsing Amazon, that an electronic version exists and is available for immediate download at a cost similar to the hardback edition.

The book takes a very practical line and whilst it outlines some of the theory, most is omitted. As such, the interested reader is likely to find Huber's Robust Regression, or Hampel et al's Robust Statistics: the Approach Based on Influence Functions good complements (and both of those titles have also been made recently available in Wiley paperback).

In the preface to the book, the authors motivate what follows with some key observations, such as "Out of the many possible regression techniques, the least

squares method has been generally adopted because of tradition and ease of computation", "Outliers occur very frequently in real data", and, importantly, "Some people think that robust regression techniques hide the outliers, but the opposite is true". This final point, that robust regression methods highlight outliers, recurs throughout the book. The basic problem with least squares regression is perhaps stated most clearly in the chapter on outlier diagnostics for least squares models: "By definition, least squares tries to avoid large residuals. Consequently, one outlying case may cause a poor fit for the majority of the data because the least squares estimator tries to accommodate this case at the expense of the remaining observations." The style here is common throughout the book. It is informal and intuitive reasoning, not pages of algebra. Where algebra is introduced, it tends to be fairly simple and is intended to aid the reader's understanding, not to provide thorough mathematical foundations.

The book contains many examples, some synthetic, but many real. The data sets are indexed in the back of the book and the authors made them available on a floppy disk. This seems rather quaint these days, and all of the data sets are available online from <http://www.uni-koeln.de/themen/Statistik/data/rousseeuw/>. Some of the example data sets contain clearly contaminated observations and it is possible to object to the authors' approach by arguing that in practice, the data analyst would have spotted the data errors and either corrected or deleted them. However, as Rousseeuw and Leroy argue, when outliers happen to be leverage points, this argument fails and least squares won't do. Moreover, in high dimensions, data become increasingly difficult to visualize and so outliers become increasingly difficult to identify.

This last point led Rousseeuw and Leroy to split the topic of robust regression into two separate chapters: Simple Regression and Multiple Regression.

Book Review by Harry Southworth (continued)

The chapter on simple regression contains several data sets in which outliers clearly exist and which the authors' preferred method, Least Median of Squares, is clearly demonstrated to accurately identify the aberrant observations. The authors motivate their choice of method on grounds of ease of computation (which is no longer an issue for most of us) and ease of explanation to clients. Several pages of these two chapters are given over to describing a FORTRAN program called PROGRESS (from *Program for robust regression*). The authors advise that it be run on a microcomputer with at least 256Kb of RAM and explain that the program is restricted to use with data sets consisting of no more than 300 observations. PROGRESS is still available for download, in both its FORTRAN source and as a compiled executable, though at least some of it has been incorporated into S-PLUS (without the memory restrictions). All of which is to say that certain parts of this book are rather out of date. However, I hasten to stress that these sections comprise a small portion of the overall text and do not at all devalue the book.

A large section of the chapter on Multiple Regression is devoted to discussing the properties of Least Median of Squares, Least Trimmed Squares and S-estimators of regression. Although several theorems and corollaries are presented, the treatment is very informal. This section also contains some remarks and observations on one-step M-estimators which gain some efficiency but lose some resistance to leverage points. A later chapter, "Algorithms", contains some related material on "Other High Breakdown Estimators" in which S-estimation is treated again and MM-

estimation (which seeks to combine the high resistance of S-estimators with the efficiency of M-estimators) is touched upon. At the time the book was written, MM-estimation was a new idea and not much space is devoted to it. The authors note, however, that S-estimation (the usual starting point of MM-estimation) is very computer intensive and that some preliminary results suggest that S-estimators do not gain anything over Least Median of Squares. Again, computation issues are no longer much of an issue, and my own experience suggests that S-estimates tend to be a bit more efficient than Least Median of Squares estimates.

One of the later chapters of the book is entitled, The Special Case of One-Dimensional Location. The chapter contains some asymptotic results and some detail of the efficiency and breakdown properties of robust estimates of location. Again, the treatment is rather informal and the interested reader might like to refer elsewhere for a more thorough treatment.

The chapter, mentioned above, on Outlier Diagnostics, introduces the familiar tools used for searching for outliers and leverage points when using least squares, such as various residuals, the hat values, Cook's distance, DFFITS and DFBETAS. The chapter describes these measures' derivation intuitively and clearly, and gives several reasons, backed up by examples, as to why these measures sometimes fail to identify aberrant observations. As a reference for these measures and as a motivation for using robust techniques, this chapter works very well.

The final chapter of the book, "Related Statistical Techniques", contains some material on robust estimation of

covariance and correlation and robust time series analysis. The material on time-series analysis deals with M-estimators which, I think, is rather out of date and has been superseded by other methodology (though I'm no kind of expert and will be happy to stand corrected).

Robust methods never made it into everyday statistical practice and there is still overreliance on classical methods. For example, it is common to characterize data by their mean and standard deviation, even though in the absence of normality (i.e. almost always) these two statistics are not very enlightening. Also, it is common to rely on least squares regression despite the method's tendency to overestimate the variance, to give misleading parameter estimates in the presence of outliers, and to hide these outliers. Presumably, as Rousseeuw and Leroy state, this is due in large part to the methods familiarity and ease of computation. In modern times, ease of computation is barely an issue, and robust methods have been implemented in some popular statistical packages. 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 rerelease of this book, and other books treating robust statistics, will rekindle some interest in this important and inappropriately overlooked subject.

References

Huber P. J. *Robust Statistics*, Wiley, 2004 (first released in 1981)

Hampel F. R., Ronchetti E. M.,

Rousseeuw P. J. and Stahel W. A. *Robust Statistics: The Approach Based on Influence Functions*, Wiley, 2005 (first released in 1986)

Book Review by Sada Nand Dwivedi (India)

Sorin Drăghici

Data Analysis Tools for DNA Microarrays

Chapman & Hall/CRC (2003) 1-58488-315-4

This book is one of the publications under Mathematical Biology and Medicine Series that aim to encourage the integration of statistical, mathematical and computational methods in biology. As indicated by the title of the book, this exclusively addresses various approaches used in analysis of data on microarrays, which contain a large number of DNA samples. This plays an important role regarding the move towards genomic research. The analytical methods developed specifically may prove to be of much use to derive appropriate and meaningful observations. As pointed out by the author, very few texts are available that deal with analytical aspects of microarrays. Further, they provide a little help to extract biologically interesting information out of the large amount of data generated in the laboratory. The author has tried to plug this gap, by producing this book, which describes in detail, the analytical tools for DNA microarrays.

The author has tried to cover the elements of genetics and molecular biology that may be necessary for statisticians, mathematicians and computer scientists. He provides a clear and rigorous description of the

algorithms without overwhelming the reader with the usual cryptic notation or with too much mathematical detail. Further, the descriptions of the few necessary statistical and mathematical facts are explained at a level that is fully accessible to the non-mathematically minded readers like biologists. Also, this book may allow a microarray user to make an informed choice as to what data analysis technique to use. Inclusion of many data sets and related worked analytical examples further adds clarity and better understanding of the used statistical methods.

This book is broadly divided into two parts. The first consists of nine chapters dealing with an overview of microarrays and to create a solid foundation by presenting the necessary elements of the statistics that constitute the building blocks of any data analysis. On the other hand, the second part consists of six chapters introducing the reader to the details of the techniques most commonly used in the analysis of microarray data. In addition, out of two more chapters, first (chapter 16) includes a few real data sets analysed with various software packages. The last chapter (chapter 17) presents some conclusions as well as a brief presentation of some novel

techniques expected to have a great impact on this field in near future. Thus the book is divided into 17 chapters, each of which starts with an introduction, outlining related topics and ends with a write-up in the form of summary before an appendix if any. At the end of the book, before presenting a subject index, a comprehensive list of all desired references is provided.

The first chapter describes various important issues like Bioinformatics, genomics, the building blocks of genomic information & the need of microarrays, and their related characteristics in a lucid and clear manner. Further, the basic structure of DNA, RNA and the process of gene expression are also described. It is made clear that genetic information flows from DNA to RNA to proteins. This will obviously help non-biologists (e.g. statisticians, mathematicians and computer scientists) to refresh their necessary biological background knowledge. In this chapter, the author summarizes that comparing the expression levels of various genes between different conditions is of extreme interest to life scientists that stimulated the development of high throughput techniques for monitoring gene expression such as microarrays.

Chapter 2 entitled "Microarrays" describes the microarray technology. For this, along with definition of the microarrays, process of its formation (e.g. probe, target, transcription) is presented. The approaches used in fabrication of microarrays (deposition of DNA fragments; in situ synthesis) are also described. While dealing with applications of microarrays, it has been reported that microarrays can be used to generate accurate, precise and reliable gene expression data. However, there are certain challenges (e.g. noise, normalization, experimental design, large number of genes, significance, biological factors and array quality assessment) in using microarrays in gene expression studies. Further, variability introduced through various steps under a microarrays experiment is described in a tabular form. This chapter forms the foundation for future chapters.

Chapter 3, "Image Processing" deals with a very short description of the basic notions involved in digital imaging followed by image processing issues specific to microarrays. This chapter is mainly aimed at life scientists or statisticians who are not familiar with the digital image processing.

The 4th (Elements of Statistics) and 5th (Statistical Hypothesis Testing) chapters describe some elementary statistics notions that may provide the biologists with a general perspective on issues related to microarrays. In addition to introducing a few necessary statistical terms (e.g. population, parameters, random variable, sample etc.), the 4th chapter discussed measures of averages, measures of dispersion, covariance & correlation, probabilities, Bayes' theorem, some commonly used probability distributions and central limit theorem. The 5th chapter introduced to formulate research and null hypothesis, types of error, p-value and its link to the level of significance and power. This chapter discusses classical hypothesis testing where as 6th chapter applies it to microarrays data analysis. This deals with basics of hypothesis testing along with parametric testing involving one or two samples. These chapters help in making an informed choice during the subsequent data analysis.

Chapter 7 presents the family of analysis of variance (ANOVA) methods that are intensively used by many researchers to analyse microarray data. To be more specific, one- and two- way ANOVA have been discussed and applied. It has been emphasized that ANOVA is a parametric approach that assumes normality. This chapter discussed the randomized block design and the factorial design ANOVA. Further, chapter 8 uses some of the ANOVA approaches in the discussion of various techniques for experimental design. The main tools used in experimental design are: replication, randomisation, and blocking. The discussion includes some of the classical experimental designs like the fixed effect design, the randomized block design, the balanced incomplete block design, the Latin square design and the factorial design. Several of the ANOVA models like those proposed by Kerr and Churchill for cDNA microarrays, as well as a related ratio-based experimental design are also discussed. The author has suggested useful references in this regard. Chapter 9 covers issues related to the fact that microarrays interrogate a very large number of genes simultaneously and its consequences regarding data analysis. This chapter discussed the issue of correcting (Sidak Correction; Bonferroni Correction; Holm's Correction) for multiple comparisons. Some of the bootstrapping methods (Permutation and SAM) are also discussed.

In the second part of the book, chapter 10 summarized the tools mainly used for exploratory analysis and visualization of microarrays data. These tools are box plots, gene pies, histograms, time series plots, Principal Component Analysis (PCA), and Independent Component Analysis (ICA). They may help in identification of relevant phenomena as well as the parameters (genes) that control them. For each tool, the discussion includes a detailed explanation of the tool as well as a discussion of its advantages as well as several potential problems that can occur in its practical use. In most case, the tools are presented using real data.

Chapter 11 also deals with most widely used advanced tools of microarrays data analysis, that is, clustering techniques. They include K-means, hierarchical clustering and self-

organizing feature maps. This procedure helps in finding groups of: (i) genes with similar expression profiles across a number of experiments and (ii) individuals with similar expression profiles within a population. Again, the purpose here is to explain the techniques in an unsophisticated yet rigorous manner. While discussing the circumstances when a particular method can be used, major emphasis is on the discussion of strengths and weaknesses of that method. Further, to clarify these points in a better way, appropriate examples have been provided.

Chapter 12 concentrates on data preparation issues that are crucial for the final results of the data mining process but are often ignored. This addresses various techniques related to the pre-processing and normalization of data to be used in an analysis. In this chapter, some methods of transforming data so that standard methods can be used are discussed. These are mainly logarithmic transformation, combining replicates and eliminating outliers and array normalization. The discussion also includes merits and demerits of these methods. Many other pre-processing techniques that are specific to a given technology are discussed. Alternatively, model-based normalization approaches also exist and have been shown to perform very well. This chapter will obviously be extremely useful both to the biologists as well as methodologists.

The methods used to select differentially regulated genes in comparative experiments are described in Chapter 13. In view of the known drawbacks of earlier existing methods (e.g. fold change; unusual ratio), there is need to use methods of classical hypothesis testing (e.g. appropriate version of the ANOVA methods) that essentially rely on a careful experimental design and the presence of replicate measurements. Chapter 14 shows how such lists of differentially regulated genes can be translated into a better understanding of the underlying biological phenomena. In contrast to the approach of looking for key genes of known specific pathways or mechanisms, global functional profiling is a high throughput approach that can reveal the biological mechanisms involved in a given condition. Onto-Express is a helpful tool in this regard. Further, the chapter 15 deals with the methods to select the best microarrays for a given biological hypothesis. Analyzing the list of genes on all existing arrays and providing information about the pathways, biological mechanisms and molecular functions represented by the genes on each array can accomplish this. For this+, Onto-Compare is an appropriate tool.

Chapter 16 deals with a very brief description of the characteristics of the software tools currently available for the data analysis of microarrays. The applications of BioDiscovery's GeneSight, S-Plus Array Analyser and the Spotfire DecisionSitespecialist with varying real data sets are discussed. Further, some of the software available from SAS and their capabilities are also discussed. On the other hand, the seventeenth chapter being a last chapter deals with miscellaneous and developing areas of microarrays data analysis. This also outlines some alternative approaches suggested for analysis of microarrays data. The author further emphasizes that a close symbiosis between biologists, computer scientists and statisticians is needed to carry out well-planned scientific study providing valid, conclusive and meaningful- results.

This book is clearly written, easy to read and comprehend the various issues related to microarrays data analysis that mainly covers descriptive statistics and hypothesis testing. Although non-parametric methods of hypothesis testing are not covered much, this book seems to serve the purpose of referral. In my opinion, one who wants to start working in this area should try to go through this book to get acquainted with related basic concepts.

References:

- M.K. Kerr and G.A. Churchill. Bootstrapping cluster analysis: Assessing the reliability of conclusions from microarray experiments. *Proceedings of the National Academy of Science USA*, Vol. 98(16), 8961 - 8965, (2001).
- M.K. Kerr and G.A. Churchill. Statistical design and the analysis of gene expression microarray data. *Genetical Research*, Vol. 77(2), 123 - 128, (2001).
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- D. C. Montgomery. *Design and Analysis of experiments*, Wiley (2001).

Book Review by Paul Johnson (USA)

Sanford Bolton and Charles Bon | Pharmaceutical Statistics: Practical and Clinical Applications (4th ed.) | Dekker [2003] 0-8247-4695-3

Bolton and Bon provide a book containing statistical applications to pharmaceutical research. The book will be of interest to the pharmaceutical scientist and students of statistics looking for a self-contained text. The book consists of 16 chapters and nine appendices. There is much material and many examples provide for interesting reading. The book may be used as a one-year course. Each chapter contains a key term section, exercises and references. Answers to the exercises are given at the end of the book.

Chapter 1 covers basic definitions and concepts. This includes the use of sample statistics, population parameters, measures of central tendency and spread. Concepts discussed include precision, accuracy and bias. Chapter 2 makes use of graphics, e.g. scatter plots, histograms and semi-logarithmic plots to describe data. Chapter 3 examines the binomial and normal probability distributions. The Poisson, Student's *t*, chi-square and *F* distributions are described. The authors discuss the use of the normal to approximate the binomial and illustrate the use of the Central Limit Theorem. Chapter 4 considers the choice of sampling techniques including simple random sampling, stratified, systematic, cluster sampling and sampling in quality control. Chapter 5 introduces statistical inference, estimation and hypothesis testing. Confidence intervals are constructed. The hypothesis tests described include 1) the testing of a single mean; 2) comparing means from two independent groups; 3) the testing of proportions; and 4) the comparison of variance in independent samples. Chapter 6 determines sample size and power calculations. The authors include sample size determination for bioequivalence studies. Sample size determinations are presented for normally distributed random variables and for binomial tests. The case when there are more than two treatments is addressed. Chapter 7 presents linear regression and correlation. The assumptions, variance estimates, confidence and prediction intervals,

analysis of residuals, weighted regression and nonlinear regression are topics included in this chapter. A drug stability study is used for an example. Chapter 8 presents the one-way and two-way analysis of variance. Multiple comparisons are considered e.g. Tukey, Scheffé, Newman-Keuls, and Dunnett's. The authors compare the analysis of covariance with other analyses and discuss the analysis of variance for pooling regression lines as related to stability data. The problem of missing data is addressed. Chapter 9 describes the factorial and fractional factorial design. The factor, levels, effects and interaction are defined. The method of Yates is illustrated by example. Chapter 10 examines methods for transforming data and finding outliers. The logarithmic and arcsine transformation are discussed in detail. The authors describe Dixon's test and the *T* method used for the identification of outliers. Chapter 11 describes experimental design in clinical trials. The authors comment that when designing clinical studies the following are important: i) absence of bias; ii) absence of systematic error; iii) adequate precision; iv) choice of patients and v) simplicity and symmetry. The authors discuss the crossover design and repeated measures designs. Chapter 12 examines quality control including the use of control charts, moving averages, acceptance sampling and operating characteristic curves. The authors describe statistical procedures in assay development. Chapter 13 examines process and assay validation. The authors ask and answer the following questions: i) are the assays within the in-house limits? ii) drug homogeneity? iii) are the average drug concentration and homogeneity in the bulk mix the same as in the final product? and iv) are batches in control based on quality control charting of averages? Chapter 14 describes computer intensive methods, including those of Monte Carlo simulation and bootstrapping. An example used is cure rate data for an antibiotic treatment. The authors conclude that both Monte Carlo

simulation and bootstrapping methods are powerful tools for solving problems. Chapter 15 explores the use of nonparametric methods. The authors discuss the use of nonparametric confidence intervals for crossover and bioequivalence studies. Tests described include: the Wilcoxon signed rank test; the Wilcoxon rank sum test; Kruskal-Wallis test; Friedman test; and the Quade test. Chapter 16 considers optimisation techniques and screening designs. The authors consider optimisation using factorial designs, optimisation of a combination drug product and the use of composite designs to estimate curvature. One example presents the results of a three-component simplex system for tablet hardness. This concludes the main section. Next follows a glossary and nine appendices, which cover: 1) some properties of the variance; 2) the comparison of slopes and testing of linearity; 3) multiple regression; 4) tables e.g. Chi-square, *t* and *F* distributions, Wilcoxon rank sum test etc. 5) outlier tests and chemical assays; 6) reasons for rejecting a batch; 7) when to average; 8) excel workbooks and SAS programs and 9) an alternative solution to the distribution of the individual bioequivalence metric.

The book makes an important contribution to the field. The book contains much material (755 pages) and is well written. The Excel workbooks and SAS programs are included on a CD-ROM, provided with the book. The book contains an extensive subject index. The figures, tables, examples, summaries, discussions and conclusions are well presented. I liked the exercises at the end of each chapter and answers are provided at the end of the book. The key term section at the end of each chapter provides a useful summary. There is a glossary provided at the end of the book. The book details the approaches used in pharmaceutical statistics. The examples provide for interesting reading. I recommend this book. It makes a worthwhile addition to any medical science, pharmaceutical science and/or statistics library.

Book Review by Aris Perperoglou (Netherlands)

S. Huet, A. Bouvier, M.-A. Poursat and E. Jolivet | Statistical Tools for Nonlinear Regression: A Practical Guide with S-PLUS and R Examples (2nd edn) | Springer (2004) 0-387-40081-8

As indicated by the title, this book is a practical guide to non-linear regression with applications in agronomy and biochemistry using S-plus and/or R software. The authors state that their intention is to present the methods in an intuitive way rather than presenting the mathematical background. Their intention is to create a "cookbook" to guide the readers when dealing with non-linear methods. They propose two uses for their text, one for applied researchers as a practical guide, and one for students as a tutorial book. This second edition includes two additional chapters presenting binomial, multinomial and Poisson models. Their strategy throughout the book is straightforward. They start by presenting practical examples and then discuss the statistical problems and ways to deal with them. At the end of each chapter they illustrate practically the use of the *nl2* software to analyse the data.

The book only assumes some basic knowledge of statistics, mainly in linear modelling and GLMs. Since it targets readers who are not familiar with statistical theory I believe that a short introduction in the usefulness of non-linear methods is lacking. The mathematical proofs are not presented, however in some cases, some technical background is presented in different fonts so the reader may skip them. The first chapter of the book introduces the datasets that are used throughout the book in the examples. There are five different problems each described in detail. The parametric non-linear model is then introduced and its estimation is discussed briefly. The *nl2* program is also introduced at the end of the chapter. The second chapter deals with the accuracy of the estimators, confidence intervals and tests, followed by the third chapter that deals with the estimation of the variance. Chapter four discusses model diagnostics with means of

graphics or list and the possible numerical troubles during the estimation process, and chapter five deals with calibration and prediction.

The last two chapters discuss binomial non-linear models and multinomial and Poisson models.

The book presents the data in detail and makes use of them in each chapter, illustrating practically how non-linear methods can be used. However, this is not a stand-alone text but just a guide. The software *nl2* is not the usual package that an S-plus user is accustomed with. Although it is well explained, judging superficially, I did not like the way it looks and work.

As the title indicates this book is very applied so an expert on non-linear regression will not find the mathematical background in it. However, I would not recommend the book to students either, as it is more like a software guide than a statistical text.

ISCB26 – Szeged 2006 – Draft Programme

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Time	Sunday 21 August	Monday 22 August	Tuesday 23 August	Wednesday 24 August	Thursday 25 August
08:00-09:00	Registration	Registration	Registration	Registration	Registration
09:00-10:30	Pre-conference courses 1, 2, 3, 4	Opening & Invited Session: Pharmacogenomics	Invited Session: Regression and prediction with many covariates Contributed Session 10 • Dose-finding methodology and control charts	Invited Session: Complex interventions in community health settings Contributed Session 11 • Sample size determination and dichotomising outcomes	Mini-symposium: Genomics-based diagnosis and prognosis
10:30-11:00	Refreshments	Refreshments	Refreshments	Refreshments	Refreshments
11:00-12:30	Pre-conference courses 1, 2, 3, 4	Invited Session: Analysis of time-varying treatment data Contributed Session 1 • Statistics in genetics I	11:00 - 12:00 Keynote Lecture 12:00 - 13:00 Annual General Meeting	Invited Session: Statistics and twin studies: a double challenge Contributed Session 12 • Meta-analysis	Mini-symposium: Genomics-based diagnosis and prognosis
12:30-14:00	Lunch	Lunch	Lunch	Lunch	
14:00-15:30	Pre-conference courses 1, 2, 3, 4	Contributed Sessions 2-5 • Survival models I • Statistics in genetics II • ROC and other methods for diagnostic studies • Miscellany	Conference Excursions	Contributed Sessions 13-16 • Essential concepts • Survival models II • Methods for longitudinal data • Medical studies	
15:30-16:00	Refreshments	Refreshments		Refreshments	
16:00-18:00	Pre-conference courses 1, 2, 3, 4	Contributed Sessions 6-9 • Methods for categorical data • Compliance and causal inference • Epidemiology • Sequential and spatial analysis		Contributed Sessions 17-20 • Clinical studies • Survival models III (competing risks, frailties) • Statistical modelling • Confounding effects	
18:00-	Choir Rehearsal	18:00-19:00 Reception in Ferenc Móra Museum		18:00-23:00 Conference Dinner at Ópusztaszer	

ISCB Executive Committee Meeting: 14:00, Sunday 21 August 2005.

Poster sessions will be held on: Monday 22, Tuesday 23 and Wednesday 24 August 2005

Sunday 21 August 2005
09:00 - 18:00
<i>Pre-conference course 1:</i> Analysis of quality of life studies in clinical trials Diane Fairclough, Denver, CO, USA
<i>Pre-conference course 2:</i> Analysis of non-compliance in clinical trials Els Goetghebeur, Bernard Vrijens and Stijn Vansteelandt, Ghent, Belgium
<i>Pre-conference course 3:</i> Spatial epidemiology Zsolt Lang and Jenő Reiczigel, Budapest, Hungary
<i>Pre-conference course 4:</i> R for Biostatistics Peter Dalgaard, Copenhagen, Denmark

ISCB Executive Committee Meeting: 14:00, Sunday 21 August 2005.

Monday 22 August 2005	
09:00 - 10:30	
Auditorium	
<i>Opening of the Conference</i>	
Invited Session 1: Pharmacogenomics Organiser: Lutz Edler (Heidelberg, Germany)	
Biostatistical modelling in functional genomics for clinical cancer research Philippe Broet (Paris, France)	
Pharmacogenomic companion studies in clinical trials on treatment responders Ulrich Mansmann (Heidelberg, Germany)	
Discussant Lutz Edler (Heidelberg, Germany)	
11:00 - 12:30	
<i>Auditorium</i>	<i>Hall A</i>
Invited Session 2: Analysis of time-varying treatment data Organiser: Robin Henderson (Newcastle, UK)	Contributed Session 1: Statistics in genetics I
The intensity-score approach to adjusting for confounding Babette Brumback (Los Angeles, CA, USA)	On genetic information and diversity Jana Zvárová (Prague, Czech Republic)
Assumptions, priors and sensitivity analysis: reality checking in causal inference and missing data problems Joe Hogan (Providence, RI, USA)	Statistical consideration of the identifications for disease-associated SNPs in whole-genome association study Yasunori Sato (Tokyo, Japan)
Estimation of optimal adaptive treatments using observational data: a regret-based approach to dynamic anticoagulation Robin Henderson (Newcastle, UK)	Predicting patient outcome from protein mass spectrometry data Lucinda Billingham (Edgbaston, Birmingham, UK)
	Assessing and evaluating pharmacogenetic evidence: a Bayesian approach Keith R. Abrams (Leicester, UK)

Monday 22 August 2005			
14:00 - 15:30			
<i>Auditorium</i>	<i>Hall A</i>	<i>Hall B</i>	<i>Hall C</i>
Contributed Session 2:	Contributed Session 3:	Contributed Session 4:	Contributed Session 5:
<i>Survival models I</i>	<i>Statistics in genetics II</i>	<i>ROC and other methods for diagnostic studies</i>	<i>Miscellany</i>
Explained variation in relative survival regression Janez Stare (Ljubljana, Slovenia)	Local False Discovery Rate estimation in functional genomic studies: A comparative study Cyril Dalmasso (Villejuif, France)	Using the Receiver Operating Characteristic curve for gauging treatment effect in clinical trials Lyndia Brumback (Seattle, USA)	Optimizing the use of information collected through electronic monitoring of patient adherence Laetitia Comté (Liege, Belgium)
Extrapolation of survival curves using relative survival models Paul Lambert (Leicester, UK)	Modelling data from serial analysis of gene expression with Poisson mixtures Helene H. Thygesen (Amsterdam, Netherlands)	Adjusting for covariate effects in biomarker studies using the subject-specific threshold ROC curve Holly Janes (Seattle, USA) <i>Conference Award for Students</i>	Early detection of outbreaks of infectious diseases Siem Heisterkamp (Bilthoven, Netherlands)
Implications of model misspecification among robust tests for recurrent events Jean-Marie Boher (Chilly-Mazarin, France)	Joint estimation of gene-gene and gene-environment interaction effects for numerous loci using (double) penalised log-likelihood Michael Tanck (Amsterdam, Netherlands)	Characteristics of two tests for detecting a resistance to the activated C-protein in the absence of a gold standard Laurence Joubin (Paris, France)	Classification of patient hospital path with symbolic data analysis: application to prediction of survival after admission for myocardial infarction Catherine Quantin (Dijon, France)
Weighted penalised logistic regression and survival analysis to estimate multilocus haplotype effects Olga Souverein (Amsterdam, Netherlands)	Serial analysis of gene expression (SAGE) – sequencing errors Vaclav Faltus (Prague, Czech Republic)	Assessment of the diagnostic tests by GEE and Latent Class Modeling H. Refik Burgut (Adana, Turkey)	A new system of linear equations with the unknowns assumed to be unobserved values of random variables Toshiro Tango (Saitama, Japan)

Monday 22 August 2005			
16:00 - 17:50			
<i>Auditorium</i>	<i>Hall A</i>	<i>Hall B</i>	<i>Hall C</i>
Contributed Session 6:	Contributed Session 7:	Contributed Session 8:	Contributed Session 9:
Methods for categorical data	Compliance and causal inference	Epidemiology	Sequential and spatial analysis
Quantification of agreement for categorical data Lene Theil Skovgaard (Copenhagen, Denmark)	Estimating the causal effect of observed exposures, measured with error in a randomized trial Els Goethgebeur (Ghent, Belgium)	Modeling smoking history using an overall indicator of exposure Karen Leffondré (Montreal, Canada)	Use of intermediate outcomes to reduce trial duration in sequential designs in stroke Anne Whitehead (Reading, UK)
Testing homogeneity in the pattern of agreement for a categorical scale in twin and reliability studies Chris Roberts (Manchester, UK)	Marginal structural models for partial treatment regimes to estimate the causal effect of nosocomial pneumonia on mortality in intensive care units Stijn Vansteelandt (Ghent, Belgium)	Demography and epidemiology: age-period-cohort models in the computer age Bendix Carstensen (Copenhagen, Denmark)	A sequential comparison of the pairwise associations within two independent groups with application in twin studies Fazil Baksh (London, UK)
Meta-analysis of clinical trials with ordinal outcome: comparison of methods Guido Knapp (Dortmund, Germany)	Comparison of structural modelling approaches to assess the effect of compliance in randomised trials Krista Fischer (Tartu, Estonia)	Seasonality of birth for acute lymphoblastic leukaemia in Southern Hungary using harmonic analysis Tibor Nyári (Szeged, Hungary)	Sequential analysis of Quality of Life measurements using mixed Rasch models Véronique Sebille (Nantes, France)
Choice of test for association in small sample unordered r x c tables Stian Lydersen (Trondheim, Norway)	Using double robust estimators of marginal structural models to adjust for non-compliance in clinical trials Richard Emsley (Manchester, UK)	Back-calculation for full clinical surveillance application to the French bovine spongiform encephalopathy (BSE) epidemic Virginie Supervie (Paris, France)	Bayesian spatial cancer survival with smoothed age, period and cohort effects Erik A. Sauleau (Mulhouse, France)
Poisson-Poisson model for zero-inflated count data: health of Indonesian children Yin Bun Cheung (London, UK)	Causal analyses under time-varying treatments Simon Bond (Cambridge, UK)	The prevalence of chronic hepatitis C in England and Wales using multi-parameter evidence synthesis Michael Sweeting (Cambridge, UK)	The use of spatial smoothing models in understanding the epidemiology of campylobacter infections Frank Dunstan (Cardiff, UK)

Tuesday 23 August 2005	
09:00 - 10:30	
<i>Auditorium</i>	<i>Hall A</i>
Invited Session 3: Regression and prediction with many covariates Organiser: Michael Schemper (Vienna, Austria)	Contributed Session 10: Dose-finding methodology and control charts
Logistic regression analysis with (quasi-) completely separated data: theory and applications Georg Heinze (Vienna, Austria)	Estimation of the Maximum Tolerated Dose in phase I trials with patient heterogeneity on genetic information and diversity Wessel van Wieringen (Rotterdam, Netherlands)
Regression on high-dimensional ordered data Paul Eilers (Leiden, Netherlands)	Flexible design and efficient implementation of adaptive dose-finding studies Christopher Weir (Glasgow, UK)
Logic regression in SNP association studies Ingo Ruczinski (Baltimore, MD, USA)	Optimal dose finding designs for bivariate outcomes Sarah Zohar (Paris, France)
	Recent advances in control chart methodology Moshe Pollak (Jerusalem, Israel)

Tuesday 23 August 2005	
11:00 - 12:00	
<i>Auditorium</i>	
<i>Keynote Lecture</i> Improving Confidence Intervals for Proportions, Differences of Proportions and Odds Ratios Alan Agresti, Gainesville, FL, USA	
12:00 - 13:00 Annual General Meeting – open to all attendees of the Szeged meeting.	
14:00 - Conference Excursions	

Wednesday 24 August 2005	
09:00 - 10:30	
<i>Auditorium</i>	<i>Hall A</i>
Invited Session 4: Complex interventions in community health settings <i>Organiser: Mike Campbell (Sheffield, UK)</i>	Contributed Session 11: Sample size determination and dichotomising outcomes
Introduction: what are complex interventions? Mike Campbell (Sheffield, UK)	Power and sample size calculations for discrete outcome scores Spyridoula Tsonaka (Leuven, Belgium) <i>Conference Award for Students</i>
A fresh look at complex interventions in primary care Pat Yudkin (Oxford, UK)	Sample size calculations for a clinical trial with more than two arms using a common control group assessing time to event – an overview of the available methods and a proposed stopping rule Anneke Grobler (Durban, South Africa) <i>Conference Award for Scientists</i>
Complex interventions in implementation research Jeremy Grimshaw (Ottawa, Canada)	Sample size formulae for the self-controlled case series method Patrick Musonda (Milton Keynes, UK)
What are the problems in using cluster randomised trials to assess complex interventions, and how to improve them Sandra Eldridge (London, UK)	Proportional odds logistic regression – effective means of dealing with limited uncertainty in dichotomizing clinical outcomes Zdenek Valenta (Prague, Czech Republic)
11:00 - 12:30	
Invited Session 5: Statistics and twin studies: a double challenge <i>Organiser: Els Goetghebeur (Ghent, Belgium)</i>	Contributed Session 12: Meta-analysis
Structural equation modelling in genetics: from epidemiology to gene discovery Dorret Boomsma (Amsterdam, Netherlands)	Quantifying heterogeneity in meta-analysis Martina Mittlböck (Vienna, Austria)
Modelling twin survival: heritability and beyond Ivan Iachine (Odense, Denmark)	Bayesian hierarchical models for informatively missing data in meta-analysis Ian White (Cambridge, UK)
Three-state frailty model for age at onset of dementia and death in Swedish twins Juni Palmgren (Stockholm, Sweden)	Graphical and cluster-analytic techniques for preliminary inspection of diagnostic test evaluation studies prior to a meta-analysis Jürgen Hilden (Copenhagen, Denmark)
Discussant Stijn Vansteelandt (Ghent, Belgium)	Modelling gene-gene-environment joint effects in meta-analysis of genetic association studies Georgia Salanti (Cambridge, UK)

Wednesday 24 August 2005			
14:00 - 15:30			
<i>Auditorium</i>	<i>Hall A</i>	<i>Hall B</i>	<i>Hall C</i>
Contributed Session 13:	Contributed Session 14:	Contributed Session 15:	Contributed Session 16:
Essential concepts	Survival models II	Methods for longitudinal data	Medical studies
Change from baseline or analysis of covariance? Lord's paradox and other matters Stephen Senn (Glasgow, UK)	Modelling overall survival in a two-stage non-mixture cure model Claire Weston (Leicester, UK)	Analysis of incomplete repeated measurement data when the cause of missingness is known Kate Walker (London, UK)	Twinning and pre-eclampsia Marie Reilly (Stockholm, Sweden)
Efficiency of the analysis of change: an empirical evaluation Maria N. Medina (Bogota, Columbia)	A reanalysis of amalgam restorations in the Royal Air Force using the Bayesian counting process approach with random effects Samuel O.M. Manda (Leeds, UK)	Model for longitudinal data subject to time dependent non-compliance Becque Taeko (Cambridge, UK)	Multi-organ system rheumatological disease: statistical analysis of outcome measures and their interrelationships Elizabeth Allen (London, UK)
Assurance in clinical trial design Michael J. Campbell (Sheffield, UK)	A flexible model for multivariate interval-censored ages of onset in twins Andrew Pickles (Manchester, UK)	The performance of random-effects models in the presence of informative cluster size Susan Charman (London, UK)	Statistical models accounting for variation in surgical trials Steffen Witte (Heidelberg, Germany)
The logistic transform for bounded outcome scores Emmanuel Lesaffre (Leuven, Belgium)	Analysis of left-censored quantitative outcome example of procalcitonin Julien Asselineau (Bordeaux, France)	Sensitivity analysis in pattern mixture models Dimitris Rizopoulos (Leuven, Belgium)	The zero-inflated negative binomial regression model with correction for misclassification: An example in caries research Samuel Mwalili (Leuven, Belgium)

Wednesday 24 August 2005			
16:00 - 17:50			
<i>Auditorium</i>	<i>Hall A</i>	<i>Hall B</i>	<i>Hall C</i>
Contributed Session 17:	Contributed Session 18:	Contributed Session 19:	Contributed Session 20:
Clinical studies	Survival models III (competing risks, frailties)	Statistical modelling	Confounding effects
The double-blind placebo-controlled clinical trial on food allergens - methodological issues rarely recognised by biostatisticians Lutz Edler (Heidelberg, Germany)	Prediction and standard errors estimation for reduced rank parameters in competing risks and multi-state models: a simulation approach Marta Fiocco (Leiden, Netherlands)	A comparison of methods for handling missing predictor values in prognostic models Gareth Ambler (London, UK)	Seasonal confounding in air pollution and health time-series studies: a sensitivity analysis Giota Touloumi (Athens, Greece)
Bias in the estimated treatment effect in randomised trials with rescue medication: a simulation study Christina Bamia (Athens, Greece)	Competing risks analyses of safety data Tim Friede (Basel, Switzerland)	Development of a prognostic model for the onset of dementia in the presence of missing observations Maarten Schipper (Rotterdam, Netherlands)	Lower and upper bounds on the correlation between treatment and instrumental variable Edwin Martens (Utrecht, Netherlands)
Bayesian estimation of false negative rate in a clinical trial of sentinel node biopsy Robert G. Newcombe (Cardiff, UK)	Modelling competing risks with frailties Sandrine Katsahian (Paris, France)	Conditional Generalised Estimating Equations for the analysis of clustered data Sylvie Goetgeluk (Ghent, Belgium)	A semi-parametric self-controlled case series model Heather Whitaker (Milton Keynes, UK)
Clustering effects in an individually randomised trial: design consideration for the “therapist effect” Andy Vail (Manchester, UK)	Correlated compound Poisson frailty model Andreas Wienke (Halle, Germany)	Robust parametric models for random effects Katherine Lee (Cambridge, UK) Conference Award for Students	New method for handling residual confounding by severity in observational studies Marie-Pierre Sylvestre (Montreal, Canada)
Regression partitioning and statistical shape analysis in prediction of sagittal intermaxillary relations in patients with complete unilateral cleft lip and palate during puberty Stanislav Katina (Bratislava, Slovakia) <i>Conference Award for Scientists</i>	A relaxation of the gamma frailty (Burr) model Aris Perperoglou (Leiden, Netherlands)	Modelling growth variation based on linear mixed models Emmanuelle Deslandes (Paris, France)	Validation of a new method for detecting confounding by indication bias in pharmaco-epidemiology Michal Abrahamowicz (Montreal, Canada)

Thursday 25 August 2005
09:00 - 10:30
Auditorium
Mini-symposium
Genomics-based diagnosis and prognosis
Organisers: Ulrich Mansmann (Heidelberg, Germany), Axel Benner (Heidelberg, Germany)
Introduction
Tracing molecular disease mechanisms in microarray
Rainer Spang (Berlin, Germany)
<i>Solid Tumours: Breast Cancer</i>
Micro-array analysis in Breast Cancer: past, present and future in clinical practice
Dimitry Nuyten (Amsterdam, Netherlands)
Mining pathways in micro-array gene-expression data sets
Hans van Houwelingen (Leiden, Netherlands)
11:00 - 12:30
<i>Hemoblastoses: AML</i>
Genomic profiling in acute myeloid leukaemia
Lars Bullinger (Ulm, Germany)
Prediction by supervised principal components
Eric Bair (Stanford, California, USA)
Discussion
Bioinformatics; a special challenge in immunogenomics
András Falus (Budapest, Hungary)

Posters

Poster sessions will be held on: Monday 22 August, Tuesday 23 August and Wednesday 24 August 2005

First Author	Title
Allan, T.	Modelling the interdependence in outcome of six diagnostic tests in the absence of a gold standard.
Belitser, S.	Markov model to analyse time-dependent patterns based on censored data
Benda, N.	Sperm count as a surrogate endpoint for male fertility control
Bera, L.G.	The optimum codification for a better statistical analysis in our vision
Biela, U.	Relationship between overweight with high waist to hip ratio and demographic, socio-economic factors and smoking in middle aged residents of Kraków Conference Award for Scientists
Billingham, L.	Eliciting prior clinical beliefs to inform Bayesian data monitoring and analysis in a phase III trial of chemotherapy in advanced non-small cell lung cancer
Börzsönyi, L.	Some new aspects of point estimations for the evaluation of the blood gas and acid-base parameters in newborn calves
Burton, A.	Designing realistic simulation studies for complex situations
Cheung, Y.B.	Non-response to a quality-of-life question on sexual life and the validity of the simple mean imputation method
Cook, J.	A meta-analysis model for a binary outcome incorporating case-series data
Cumming, J.	Variable selection using principal components and partial correlation
Enachescu, C.	Statistical methods for osteoporosis risk estimation. Application to a clinical study. Conference Award for Scientists
Endo, A.	An allocation method for balancing prognostic factors among treatment groups using the Kullback-Leibler information
Fazekas, M.	Analysing Hungarian mortality rates and acute childhood lymphoid leukaemia Conference Award for Scientists
Fodor, K.	Biometrical evaluation of the development stages of growing rabbits and estimation of the body composition on the basis of the body measures before slaughtering
Gao, F.	On the application of the von Mises distribution and angular regression methods to investigate the seasonality of disease onset
Genc, Y.	Closed form methods to compare two proportions for clustered data
Gillies, C.	Issues in evidence synthesis for comprehensive decision models: an illustration using impaired glucose tolerance
Heinzl, H.	A case of technical uncertainty
Hiller, L.	L_{CAT} : A multivariate confirmatory construct validity statistical test for equality of dependent correlation coefficients within domain-based questionnaires
Jurkowski, B.	Assessment charts of constituent and combined classifiers performance for asthma and schizophrenia diagnosis Conference Award for Scientists
Kalmár, L.	Human papillomavirus infection and cervical intraepithelial neoplasia in a cohort of low-risk women
Klersy, C.	Analysis of competing risks allows to uncover the protective effect of a cardioverter defibrillator combined to a cardiac resynchronization device in patients with moderate to severe heart failure
Kundt, G.	A simple alternative to “mixed randomisation” by Schulz and Grimes
Kundt, G.	Incidence, therapy and prognosis of colorectal cancer in different age groups. A population-based cohort study of a cancer registry in Northern Germany
Mihalache, C.	Biostatistics correlations applied in the study of the renal artery

First Author	Title
Mihalache, M.	Epidemiology and aetiology of nosocomial infections in Sibiu's Clinical Hospital
Misztal, M.	A proposal for using logistic regression trees to identify risk subgroups among patients undergoing coronary artery bypass grafting
Newcombe, R.G.	A deficiency of the odds ratio as a measure of effect size
Panaiteescu, E.	Generalisation of control through selection planes
Parrinello, G.	Combined endpoints in clinical studies: power via simulation
Pedrono, G.	A new endpoint formulation improving clinical relevance and statistical power in vaccine trials
Piotrowski, W.	The influence of blood pressure on the risk of cardiovascular death in Warsaw POL-MONICA population during 14-years observation
Rossa, A.	Classification trees based on ROC curves
Schievano, C.	Statistical methods to study hearing impairment in a selected population
Schipper, M.	Sequential analysis as an efficient test for linkage
Shcherbatyy, M.	Fitting models and parameter estimation for delay differential equations
Simmonds, M.	Treatment effect estimates for time-to-event data and their misinterpretation
Soleymani, B.	Study of association between different characteristics of death in Isfahan city during years 2002-2003, by the use of loglinear models
Solymosi, N.	Finding spatial barriers by Monmonier's algorithm Conference Award for Scientists
Suganami, H.	A new approach of diurnal variation analysis of intraocular pressure in normal-tension glaucoma using a circular linear mixed effect model.
Sypsa, V.	Assessment of a model for hepatitis B and C viral dynamics during treatment with non-constant efficacy
Szabó, F.	Effect of a pulsating electromagnetic field therapy on plasma cortisol level, blood gases, and acid-base parameters in normal horses
Takagi, Y.	Construction of a two-stage or three-stage group sequential design with uniformly high power function
Tazhibi, M	Determination and application of proportional hazards model for survival times data of acute leukemia in Isfahan
Vágó, E.	Ridge regression method to logit model
Valet, F.	Log-linear heterogeneous association models for agreement between two ratings on an ordinal scale
Valsecchi, M.G.	A model for the implementation of international trials in rare disease
Vernic, V.C.	Multivariate analysis of the factors involved in smoking and drinking in an adolescent population Conference Award for Scientists
Walter, S.	Estimating treatment acceptability and efficacy in compliant patients
Wang, D.	Finding the best QT correction formula using the ACE algorithm
Wood, A.	Estimating and modelling regression dilution ratios in meta-analyses
Yamaoka, K.	Concordance between meta-analyses and a mega-trial: examples from the dietary education for preventing type 2 diabetes
Zadkarami, M.R.	Applied shared frailty model to evaluating the effect of Vitamin C on the rate passive memory
Zadkarami, M.R.	Factors associated with birth weight - an application of the skew-normal regression
Zajacova, P.	LM and GLM in statistical analysis of relationship between anthropological measurements and variables of surviving in cystic fibrosis patients in Slovakia
Zohar, S.	Small sample robustness of the continual reassessment method
Zoubeidi, T.	Estimation of variance components with fixed precision

Books for Review by Harry Southworth

Books for review:			
Author(s)	Title	Publisher (year) ISBN	Reviewer
1. 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	
2. Daniel Sorensen and Daniel Gianola	Likelihood, Bayesian, and MCMC Methods in Quantitative Genetics	Springer (2002) 0-387-95440-6	
3. Ettore Marubini and Maria Grazia Valsecchi	Analysing Survival Data from Clinical Trials and Observational Studies	Wiley (1995) 0-470-09341-2	
4. George G. Woodworth	Biostatistics: A Bayesian Introduction	Wiley (2004) 0-471-46842-8	
5. Gerlad van Belle, Lloyd D. Fisher, Patrick J. Heagerty and Thomas Lumley	Biostatistics: A Methodology for the Health Sciences (2nd edn)	Wiley (2004) 0-471-46842-8	
6. Eric Vittinghoff, David V. Glidden, Stephen C. Shiboski, Charles E. McCulloch	Regression Methods in Biostatistics: Linear, Logistic, Survival and Repeated Measures Models	Springer (2005) 0-387-20275-7	
7. Stephanie Green, Jacqueline Benedetti and John Crowley	Clinical Trials in Oncology (Second Edition)	Chapman & Hall/CRC, (2003) 1-58488-302-2	
8. Byron Jones and Michael G. Kenward	Design and Analysis of Cross-Over Trials (Second Edition)	Chapman & Hall/CRC, (2003) 0-412-6-640-2	
9. Mark Woodward	Epidemiology: Study Design and Data Analysis (Second Edition)	Chapman & Hall/CRC, (2005) 1-58488-415-0	
10. Julian J. Faraway	Linear Models with R	Chapman & Hall/CRC, (2005) 1-58488-425-8	
11. David Collett	Modelling Survival Data in Medical Research (Second Edition)	Chapman & Hall/CRC, (2003) 1-58488-325-1	
12. Jean Dickinson Gibbons and Subhabrata Chakraborti	Nonparametric Statistical Inference (Fourth Edition)	Chapman & Hall/CRC, (2003) 0-8247-4052-1	
13. M. M. Desu and D. Raghavarao	Nonparametric Statistical Methods for Complete and Censored Data	Chapman & Hall/CRC, (2004) 1-58488-319-7	
14. John Aitchison, Jim W. Kay and Ian J. Lauder	Statistical Concepts and Applications in Clinical Medicine	Chapman & Hall/CRC, (2005) 1-58488-208-5	
15. Warren J. Ewens and Gregory R. Grant	Statistical Methods in Bioinformatics: An Introduction	Springer, (2005) 0-387-40082-6	
16. John Verzani	Using R for Introductory Statistics	Chapman & Hall/CRC, (2005) 1-58488-450-9	
Books reviews in this issue:			
Author(s)	Title	Publisher (year) ISBN	Reviewer
1. Shein-Chung Chow & Jen-Pui Liu	Design and Analysis of Clinical Trials: Concepts and Methodologies (2 nd ed.)	John Wiley [2004] 0-471-24985-8	Friederike Barthel, UK
2. Sorin Drăghici,	Data Analysis Tools for DNA Microarrays	Chapman & Hall/CRC (2003) 1-58488-315-4	Sada Nand Dwivedi, India
3. Sanford Bolton and Charles Bon	Pharmaceutical Statistics: Practical and Clinical Applications (4 th ed.)	Dekker [2004] 0-8247-4695-3	Paul Johnson, USA
4. S. Huet, A. Bouvier, M.-A. Poursat and E. Jolivet	Statistical Tools for Nonlinear Regression: A Practical Guide with S-PLUS and R Examples (2 nd edn)	Springer (2004) 0-387-40081-8	Aris Perperoglou, Netherlands
5. Richard M Simon, Edward L Korn, Lisa M McShane, Michael D Radmacher, George W Wright, Yingdong Zhao	Design and Analysis of DNA Microarray Investigations	Springer [2003] 0-387-00135-2	Victor Moreno, Spain
6. Peter J. Rousseeuw and Annick M. Leroy	Robust Regression and Outlier Detection	Wiley (2004) 0-471-48855-0	Harry Southworth, UK
Books reviews the next 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. Andrew B. Lawson et al	Disease Mapping with WinBUGS and MLwiN	John Wiley [2003]	Maciej Gorkiewicz, Poland
3. Geoffrey J. McLachlan	Discriminant Analysis and Statistical Pattern Recognition	Wiley (2004) 0-471-69115-1	Denis Enachescu, Romania

Books for Review (continued)

Books recently sent for review:			
Author(s)	Title	Publisher (year) ISBN	Reviewer
1. John P. Klein and Melvin L. Moeschberger,	Survival Analysis: Techniques for Censored and Truncated Data	Springer (2003). 0-387-95399-X	Sarah White, Malawi
2. 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
3. J M Bernardo et al (eds.)	Bayesian Statistics 7	Oxford University Press (2003) 0-19-852615-6	Stefan Tigan, Romania
4. 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
5. Margaret Sullivan Pepe	The Statistical Evaluation of Medical Tests for Classification and Prediction	Oxford (2003) 0-19-850984-7	Jacques Jamart, Belgium
6. Sylvia Wassertheil-Smoller	Biostatistics and Epidemiology (3rd edn)	Springer (2004) 0-387-40292-6	Faans Steyn, South Africa
7. George A. F. Seber	Multivariate Observations	Wiley (2004) 0-471-69121-6	Elzbieta Pleszczyńska, Poland
8. J. Edward Jackson	A User's Guide to Principle Components	Wiley (2003) 0-471-47134-8	Nicole Close, USA
9. David A. Belsley, Edwin Kuh and Roy E. Welsch	Regression Diagnostics	Wiley (2004) 0-471-69117-8	Ulrich Mansmann, Germany
10. Harvey Motulsky and Arthur Christopoulos	Fitting models to biological data using linear and nonlinear regression	Oxford (2004) 0-19-517180-2	Tiberiu Postelnicu, Romania
11. G. A. F. Seber and C. J. Wild	Nonlinear Regression	Wiley (2003) 0-471-47135-6	Corina Violeta Vernic, Romania
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. Mikel Aickin	Causal Analysis in Biomedicine and Epidemiology: Based on Minimal Sufficient Causation	Marcel-Dekker (2002) 0-8247-0748-6	Rosa Jiménez
3. Martin J Crowder	Classical Competing Risks	Chapman&Hall/CRC (2001) 1-59488-175-5	Dario Gregori
4. Michael Finkelstein, Bruce Levin	Statistics for Lawyers (2 nd ed.)	Springer (2001) 0-387-95007-9	David A. Sclar
5. Kirkwood	Essentials of Medical Statistics	Blackwell	Dick Bezemer
6. Michael Healy	Matrices for Statistics	Oxford (2000)	Istvan Janosi
7. Shein-Chung Chow & Jen-Pei Liu	Design and Analysis of Bioavailability and Bioequivalence Studies	Marcel-Dekker (2000)	Graham Kimber
8. Donald C Monkhouse & CT Rhodes (Eds.)	Drug Products for Clinical Trials	Marcel Dekker (1998)	Koos Lubsen
9. CF Jeff Wu & Michael Hamada	Experiments: Planning, Analysis, and Parameter Design Optimisation	John Wiley (2000)	Gilg Seeber
10. Peter Armitage (ed)	Encyclopedia of Biostatistics: Vol. 4: Med-Pre	John Wiley (1998)	Aurelio Tobias

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.).

ISCB GENERAL INFORMATION

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The prices are: Full A4 page: € 500 Half A4 page: € 300 Quarter A4 page: € 200	Additionally, we will include loose flyers with the distribution of the newsletter at an initial handling cost of € 500. However, if the addition of the flyers increases the postal charges, the advertiser will also be charged the difference in distribution costs. For further information, please contact the ISCB Office.
Publishing dates: Dec 2005 (and deadlines) Jun 2006	early Nov 2005 early May 2006
Adverts sent to the ISCB emailing list of approximately 800 current and recent members:	€ 750 for 4 emails/year € 300 for a single email
ISCB webpage advertising:	€ 750 for one year with Link from ISCB's homepage

IMPORTANT NOTE: Email Lists and Personal Information

ISCB has a strict policy not to give out any information concerning its members to **any** organisation which requests it. If a company wishes to send material to the members, the brochures must be sent to the Society's Permanent Office and News Editor for distribution with the News (see above). Alternatively, small non-commercial announcements can be sent free of charge as an email to most members of ISCB.

Society's Aims

The Society is organised and shall be operated for educational and scientific purposes with the following Aims:

- to stimulate research on the biostatistical principles and methodology used in clinical research;
- to increase the relevance of statistical theory to clinical medicine;
- to promote high and harmonised standards of statistical practice;
- to work with other societies and organisations in the advancement of biostatistics;
- to promote better understanding of the use and interpretation of biostatistics by the general public, and by national and international organisations and agencies within the public and commercial sectors with an interest in, and/or responsibilities for, public health; and
- to provide a common forum for clinicians and statisticians through meetings, seminars and publications

Changes of Address or Email

Please inform the Permanent Office that looks after the membership and mailing list databases. Also, if your **email address changes**, please inform the Office and the News Editor so that your address is changed in the ISCB database and emailing list (yahoogroup).

Information on Submitting Articles

Articles sent via email or on diskette (Word, HTML or text) on almost any topic are most welcome. This is an informal newsletter for you the readers, so please join in and make ISCB News a magazine that's even more interesting and fun to read.

How to Contact the ISCB Office and Executive Committee

Who	Address	Tel:	Fax:	Email:
ISCB Permanent Office	P.O. Box 130, Datavej 24, DK-3460 Birkerød, Denmark	+45 4567 2279	+45 7022 1571	office@iscb.info
President: John Whitehead (UK)	MPS Research Unit, The University of Reading, PO Box 240, Earley Gate, Reading RG6 6FN, UK	+44 118 9318027	+44 118 9753169	j.r.whitehead@reading.ac.uk
Vice-President: Emmanuel Lesaffre (B)	Catholic University Leuven, Biostatistical Centre, U.Z. St. Rafael, Kapucynenvoer 35, B-3000 Leuven, Belgium	+32 16 336 896	+32 16 336 900	emmanuel.lesaffre@med.kuleuven.ac.be
Secretary: Harbajan Chadha-Boreham (CH)	Rue Porot, F-21440 Francheville, France	+33 3 80 35 17 59		Harbajan.Chadha-Boreham@Actelion.Com
Treasurer: Norbert Victor (D)	Institut für Medizinische Biometrie und Informatik, Im Neuenheimer Feld 305, D-69120 Heidelberg, Germany	+49 6221 56 4140	+49 6221 56 4195	victor@imbi.uni-heidelberg.de
News Editor: David W. Warne (CH)	Chemin du Petit-Bel-Air 115, CH-1226 Thônex, Switzerland	+41 22 700 6380 +41 22 739 3374		david_w_warne@bluewin.ch
Webmaster: Bjarne Nielsen (DK)	Medicon Biometrics A/S, P.O. Box 130, Datavej 24, DK-3460 Birkerød, Denmark	+45 4567 2278	+45 7022 1571	bn@medicon.dk
Past-President: Maria Grazia Valsecchi (I)	Dept. of Clinical Medicine and Biotechnology, University of Milano, Bicocca, Via Cadore 48, I-20052 Monza, Italy	+39 039 233 3074	+39 039 233 2314	grazia.valsecchi@unimib.it
Peter Lachenbruch	US Food and Drug Administration, OBE/DB HFM-215, 1401 Rockville Pike, Rockville, MD 20852, USA	+1 301 827 6055	+1 301 827 3529	lachenbruch@cber.fda.gov
Rumana Omar	University College London, Statistical Science, Gower Street, London WC1E 6BT, United Kingdom	+44 20 76791877		Rumana@stats.ucl.ac.uk
Catherine Quantin	Service d'Informatique, Médicale & Biostatistique, D.I.M., C.H.U. de Dijon, Hopital du Bocage, BP 77908, F-21079 Dijon Cedex, France	+33 3 80 29 34 65	+33 3 80 29 39 73	catherine.quantin@chu-dijon.fr
Jeno Reiczigel	Szent Istvan University, Faculty of Veterinary Science, Dept. of Biomathematics & Informatics, Istvan ut 2, H-1078 Budapest, Hungary	+36 1 478 4215	+36 1 478 4217	jreiczig@univet.hu
Marie Reilly	Karolinska Institute, Medical Epidemiology & Biostatistics, Nobelsväg 12a, Box 281, S-171 77 Stockholm, Sweden	+46 852 483982	+46 8 314975	Marie.Reilly@meh.ki.se
Martin Schumacher	Institute of Medical Biometry & Medical Informatics, Stefan-Meier-Str. 26, D-79104 Freiburg, Germany	+49 761 203 6661	+49 761 203 6680	ms@imbi.uni-freiburg.de
Vassiliki-Anastasia Sypsa	Athens University Medical School, Dept. of Hygiene & Epidemiology, M. Asias 75, GR-11527 Athens, Greece	+30 210 7462193	+30 210 7462190	vsipsa@cc.uoa.gr
Koos Zwinderman	Academic Medical Centre, Dept. of Clinical Epidemiology & Biostatistics, University of Amsterdam, PO Box 22660, NL-1100 DD Amsterdam, Netherlands	+31 20 5665820	+31 20 6912683	a.h.zwinderman@amc.uva.nl

How to Contact the ISCB Subcommittees

Please contact the chairs of these subcommittees for further information.

Title & Email	Terms of Reference	Members	Email addresses
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 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)	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
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)	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
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: Carol Redmond (USA) Members: Mike Campbell (UK), Havi Murad (ISR) Rumana Omar (UK), Elisabeth Svensson (S), Nicole Close (USA), Maria Grazia Valsecchi (I)	ckr3@pitt.edu m.j.campbell@sheffield.ac.uk havim@gertner.health.gov.il Rumana@stats.ucl.ac.uk elizabeth.svensson@esi.oru.se nclose@emmes.com grazia.valsecchi@unimib.it
National Groups Isccb-national-groups@ yahoogroups.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), Simon Day (UK), Siem Heisterkamp (NL), Ewa Kawalec (PL), Julia Singer (H), Norbert Victor (D), John Whitehead (UK)	Michael.schemper@meduniwien.ac.at biganzoli@istitutotumori.mi.it simon.day@mhra.gsi.gov.uk SH.Heisterkamp@rivm.nl mxkawale@cyf-kr.edu.pl Julia.Singer@sanofi-aventis.com j.r.whitehead@reading.ac.uk victor@imbi.uni-heidelberg.de
Statistics in Regulatory Affairs iscb-reg-aff@ yahoogroups.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), Karsten Schmidt (DK) Harbajan Chadha-Boreham (CH), Anna Petroccione (I) Martin Schumacher	Jorgen.seldrup@quintiles.com Stephen@stats.gla.ac.uk hsimbe@med.uni-marburg.de kls@dadlnet.dk Harbajan.Chadha-Boreham@Actelion.Com anna.petroccione@nervianoms.com ms@imbi.uni-freiburg.de
Student Conference Awards iscb-stud-conf-awrd@ yahoogroups.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), Simon Day (UK), Jan Lanke (S), Vassiliki-Anastasia Sypsa (GR)	Marie.Reilly@meb.ki.se Mark.Buyse@iddi.com cesana@med.unibs.it simon.day@mhra.gsi.gov.uk jan.lanke@stat.lu.se vsipsa@cc.uoa.gr

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. Each meeting includes a mini-symposium devoted to a particular medical or statistical field. Recent topics have included Assessment of drug risks, Statistical challenges in paediatric research, Cancer genetics, Human fertility and fecundity, Emerging issues in clinical trial data monitoring, and Genetics and Epidemiology of Thrombosis.

Meetings in recent years have been held in Heidelberg (1999), Trento (2000), Stockholm (2001), Dijon (2002), London (2003) and Leiden (2004). 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. Recent courses have included Mapping and risk assessment, Statistical methods in genomics and computational biology, Introduction to frailty models, Developing and validating clinical prediction models, Design and analysis of studies with incomplete data, Smoothing and generalised additive models, Event history analysis, Introduction to genetic epidemiology, Adaptive and sequential procedures

for clinical trials, Methods of interval censored data, Issues and controversies in data analysis, Sequential Monitoring: Practical implementation of sequential designs for phase III clinical trials, Coping with missing outcome data, Essentials of clinical trials, Statistical validation of surrogate endpoints in clinical trials, Multi-state modelling, Statistical Methods for Planning and Analysis of Equivalence / Non-Inferiority Trials, Analysis of multivariate survival data and Statistical Refereeing for Medical Journals.



The composition of the **Executive Committee (ExCom)** for 2005 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), Jenő Reiczigel (H), Marie Reilly (S), Martin Schumacher (D), Vassiliki-Anastasia 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 2005) 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
2005 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 2005): Euros (EUR) 40.00 (please tick only one) <input type="checkbox"/> Full-time Student Membership of ISCB (to 31 December 2005): Euros (EUR) 20.00 (students should provide a letter from their supervisor or head of department)			
Have you previously been a member of ISCB? <input type="checkbox"/> Yes <input type="checkbox"/> No			
PAYMENT IS MADE BY:			
Credit Card Authorisation: <input type="checkbox"/> VISA <input type="checkbox"/> VISA Electron <input type="checkbox"/> Master Card <input type="checkbox"/> Euro Card <input type="checkbox"/> Maestro <input type="checkbox"/> 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	Expiry date (MM/YY): _____
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: Please transfer direct to: Barclays Bank plc PO Box 69 121 Queen Street Cardiff CF1 1SG UK		<input type="checkbox"/> Euro Account No. 6687 4511 Bank Sort Code: 20-54-78 IBAN: GB28 BARC 2018 1566 8745 11 SWIFT/BIC: BARCGB22	
Please return this form either by Email to: or by post to:		office@iscb.info ISCB Permanent Office P.O. Box 130 Datavej 24 DK-3460 Birkerød Denmark +45 4567 2279 +45 7022 1571	
Tel: Fax:			

Calendar

21-25 August 2005

Szeged, Hungary

ISCB26
Info: Julia Singer email: Julia.Singer@sanofi-aventis.com, web: <http://www.congresstravel.hu/iscb>

27-31 August 2006

Geneva, Switzerland

ISCB27
Info: David W Warne email: david_w_warne@bluewin.ch, web: <http://www.iscb2006.info>



For the latest conference info, see:

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



2005	
Jul 18 - 21	Statistics in Healthcare. Joint Conference of the Royal Statistical Society and PSI (Statisticians in the Pharmaceutical Industry), Cardiff City Hall, Wales. Information: Paul Gentry Phone: +44(0)20 7614 3918 Fax: +44(0)20 7614 3905 Email: conference@rss.org.uk Website: www.rss.org.uk/rsspsi2005
Jul 18 - 22	Workshop "Perspectives in Modern Statistical Inference III", Mikulov, Czech Republic: A satellite to the 25 th EMS in Oslo, a part of the ESF Scientific Network. It will focus on the recent results in parametric, semiparametric and nonparametric statistical inference, presented by outstanding specialists in the area. Information: Jana Jureckova, Charles University in Prague Email: jurecko@karlin.mff.cuni.cz Fax: +420 222323316 Website: http://www.math.muni.cz/workshop_2005
Jul 24 - 28	The 25 th European Meeting of Statisticians (EMS), Oslo, Norway. Information: EMS 2005, P.O. Box 114 Blindern, N-0314 Oslo, Norway Fax: (+47) 22 69 7660 E-mail: frigessi@nr.no , ems2005@nr.no Website: www.ems2005.no
Aug 7 - 11	The 2005 Joint Statistical Meetings to be held in Minneapolis, Minnesota, USA. This Meeting includes an IASSE Invited Paper Session on "Publishing in Statistics Education Journals: Views from the Editors", featuring representatives from the publications <i>Statistics Education Research Journal</i> , <i>Journal of Statistics Education and Teaching Statistics</i> . Information: Carol Joyce Blumberg Website: http://www.amstat.org/meetings/jsm/2005/index.cfm
Aug 22 - 27	The 14 th European Young Statisticians Meeting will be held in Debrecen, Hungary. Information: Local Organiser is Katalin Varga E-mail: varga@szit.bme.hu , vkati@hu.inter.net
Sep 18 - 21	International conference Applied Statistics 2005 will be held in Ribno (Bled), Slovenia. The main goal of the conference is to provide an opportunity for researchers from various statistical and related fields to come together, present their research, and learn from each other. Cross-discipline and applied paper submissions are especially welcome. Information: Andrej Blejec, Phone: +386 1 423-33-88 Fax: +386 1 257-33-90 E-mail: info.AS@nib.si Website: http://ablejec.nib.si/AS2005
Sep 26 - 27	The Biopharmacy and Health group of the SFDS organizes the 5 th International Meeting on Statistical Methods in Biopharmacy (Paris, France) with Statistical Innovations in Clinical Trials. Will genetics revolutionize clinical trials? Can better or earlier endpoints be identified? When are Bayesian approaches useful in clinical trials? Is re-sampling useful to plan and analyze clinical trials? Information: Sylvain Nicolas, Chairman - sylvain.nicolas@aventis.com and Karen Fanouillere, Secretary - karen.fanouillere@fr.netgrs.com Website: http://www.sids.asso.fr/groupe/annonce_congres.html

Oct 5 - 8	Workshop on Statistics in Genomics and Proteomics, to be held in Hotel Estoril Eden, Monte Estoril, Portugal. The workshop will aim to bring together the leading researchers in the areas of statistics in genomics and proteomics, to describe the state of the art and also to present problems that will change the next generation of biostatistics and bioinformatics researchers. Information: Lisete Sousa Phone: 00351-217500235 Fax: 00351-217500120 E-mail: lmsousa@fc.ul.pt Website: http://wsgp.deio.fc.ul.pt
Oct 25 - 28	22 nd Statistics Canada annual International Symposium "Methodological Challenges for Future Information Needs" will take place at the Crowne Plaza Hotel in Ottawa. This event will address issues of statistical methodology relevant to the work of a government statistical agency as well as to a broader statistical community including universities, industry and other organizations. E-mail: symposium2005@statcan.ca Website: http://www.statcan.ca/english/conferences/symposium2005 (in English) OR http://www.statcan.ca/francais/conferences/symposium2005 (en Français)
Oct 28 - 31	3 rd IASC World Conference on Computational Statistics and Data Analysis to be held in the Amathus Beach Hotel, Limasol, Cyprus. The Conference intends to enhance the visibility and reputation of the IASC journal, CSDA . In addition, it will establish new initiatives that will make the CSDA the leading journal in the field. Website: http://www.csdassn.org/europe/csd2005/
Dec 15 - 17	The 5 th IASC Asian Conference on Statistical Computing is to be held in Hong Kong, China. The Conference provides a forum for participants to share their knowledge in statistical computing which provides a link between statistical theory and applied statistics. Information: Wing K. Fung (Conference Chair) Phone: (852) 2859-1988 Fax: (852) 2858-9041 E-mail: lascAsian05@hku.hk Website: http://www.hku.hk/statistics/lascAsian05
Dec 27 - 31	International Statistics Conference "Statistics in the Technological Age", to be held at Cititel Mid Valley, Kuala Lumpur, Malaysia. This Conference aims to bring together eminent statisticians to discuss and present their research findings and applications of statistics in the technological age. Information: Secretariat International Statistics Conference Phone: +60-3-79674207 Fax: +60-3-79674143 E-mail: isc_malaysia@um.edu.my Website: http://iscm.math.um.edu.my
2006	
Jan 11 - 13	Fifth International Symposium on Business and Industrial Statistics, to be held in Lima, Peru. To provide a forum for exchanging ideas in statistical methods applicable to industry and business. To foster international collaboration in research and other technology transfer activities. To provide an opportunity for dialogue between statisticians in Latin America and the international community. Information: Geoff Vining E-mail: vining@vt.edu Website: http://kitchen.stat.vt.edu/~vining/isbis5/

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 E-mail: bellhouse@stats.uwo.ca Phone: (519) 661-3614 Fax: (519) 661-3813
Jul 2 - 7	ICOTS-7: <i>Working Cooperatively in Statistics Education</i> , Seventh International Conference on Teaching Statistics, to be held 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
Jul 12 - 14	Methodology of Longitudinal Surveys (MOLS) 2006: An IASSE -sponsored international conference focusing on methods for longitudinal and panel surveys, to be held at the University of Essex, United Kingdom. Phone: +44 1206 872957 E-mail: MOLS2006@essex.ac.uk Website: http://www.iser.essex.ac.uk/ulsc/mols2006
Jul 16 - 21	XXIII rd International Biometric Conference to be held in Montreal, Quebec, Canada. Website: http://www.ibt2006.org
Jul 24 - 28	26 th European Meeting of Statisticians, Thorun, Poland. Information: Adam Jakubowski (Chairman of the Local Organising Committee) Website: www-m4.mathematik.tu-muenchen.de/m4/erc/ , http://www.ems2006.umk.pl
Aug 6 - 10	Joint Statistical Meeting, to be held in Seattle, Washington
Aug 27 - 31	ISCB27 Ge06-27 th Meeting of the International Society for Clinical Biostatistics Geneva 2006 Information: David W Warne Fax: +41 22 700 6380 E-mail: david_w_warne@bluewin.ch
Aug 28 - Sep 1	COMPSTAT 2006: The 17 th Conference of the International Association for Statistical Computing (IASC) will be held in Rome, Italy. First announcement and call for papers is February 2005. E-mail: compstat2006@uniroma1.it Website: http://w3.uniroma1.it/compstat2006
2007	
Aug 22 - 29	International Statistical Institute, 56th Biennial Session: Includes meetings of the Bernoulli Society, the International Association for Statistical Computing, the International Association of Survey Statisticians, the International Association for Official Statistics and the International Association for Statistical Education, to be held in Lisboa, Portugal. Information: ISI Permanent Office, 428 Prinses Beatrixlaan, P.O. Box 950, 2270 AZ Voorburg, The Netherlands. Phone: +31-70-3375737 Fax: +31-70-3860025 E-mail: isi@cbs.nl