International Society for Clinical Biostatistics News

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Editorial

Looking back through my ISCB files, I've noticed how little paper I store these days – the days of receiving letters and faxes seems a thing of the past. Instead, everything is e-based, mainly e-mails but also webpages. So is everything better ? Yes, except when I found my old computer was doing more than normal to annoy me: its e-mail system had lost several weeks' unanswered correspondence. So my apologies if I've not replied to a message you sent me. From now on, everything's going to be backed up, and I've changed to a new pc with Windows 2000. Fingers crossed…

"Juni week was in May," to misquote myself from a couple of previous June ISCB Newsletters. In this issue you'll find details of the Stockholm conference being organised by Juni Palmgren and Simon Thompson and their local and scientific programme committees. It looks like being a very interesting conference with a lot of excellent speakers.

Thanks to the other contributors to this News: the numerous book reviewers, our book review reviewer, Caroline Jackson, and Harbajan Chadha-Boreham and Stephen Senn for an update on Dijon 2002, and Simon Day.

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The President's Bit

From Simon Day

Many thanks to Nancy Geller for guiding ISCB through 1999 and 2000 and for passing on to me a thriving and exciting Society and, not least, one that keeps its President very busy. And we all have day jobs to do as well! The hand-over went very smoothly, thanks to a lot of support from Nancy but we have quite a new Executive Committee (six new Ordinary Members), although all of the Officers have served on the Executive for at least two years. I particularly welcome the new members and hope they will work at least as hard for the Society as the retiring members have done (and in some cases, still are doing).

Although being President is a more time consuming task than I expected, it is a bit like being a 'classic' manager: you don't actually 'do' much but you do a lot of making sure other people do the 'doing'. Fortunately, some of the 'doers' (really the members and particularly Chairs of the subcommittees) are doing just fine without me. In fact, most of ISCB would get by quite well for the first few months of a new President's reign (what else do I call it?) because everything is still running off the back of the previous President. [I write this on the day of the general election in the UK and, of course, things are different in politics. Events in the first months of a new (if that's what we get) government can be clearly separated into two types: those good things that are a result of the incoming government's new policies and those bad things that are the fault of the outgoing government's policies. If only everything else in life were so simple!]

But at this time of year (no, nothing to do with political elections) we in ISCB are preparing for the conference in Stockholm and trying to gather material for this edition of the News. And it is frantic! It has been the last few years as well (I'm sure my predecessors won't mind me saying that). Emmanuel Lesaffre (our new Secretary) has quite clearly pointed out that we ought to get an outline timetable together so that we are not scrabbling around at the last minute trying to make sure everything for Executive Committee, AGM, elections, etc. is in place. We'll work on that one—but it will have to wait for the crisis to end.

And so we look forward to meeting in Stockholm (I seek sympathy because *I'm* busy… but I bet not as busy as Juni Palmgren!) I've never been to Stockholm but Scandinavia is one of my favourite areas so I am sure I will enjoy myself. By the time you read this, the programme will be complete and you can view the whole lot on the web site (easiest way is to get there via our home page: www.iscb-homepage.org). I hope to see many of you at the meeting. But let's not forget that the Dijon team for 2002 and the joint team (with the Society for Clinical Trials) for the London meeting in 2003 are already very busy. In 2004 we will meet in Leiden - the venue is already booked. And we are now considering proposals for 2005. There's a lot to look forward to! So I'll see you in some fine city or another!

As ever, please don't hesitate to contact me (or any member of the Executive Committee) about any aspects of what ISCB is - or is not - doing. I welcome your input and ideas.

Book Review by Sadik Khuder (USA)

Design and analysis of cluster randomization trials in health research, by Allen Donner & Neil Klar, Arnold (2000)

Cluster randomization trials (CRT) have become widely popular in health research and particularly in the evaluation of non-therapeutic interventions. This book is intended to be used as a reference source for investigators in the planning or analysis stage of CRT. Although relatively small, containing only 178 pages, this book is dense with information on nearly all aspects of CRT in health research.

The introductory chapter briefly discusses the basic issues in CRT. Many principles are addressed here, including the need for RCT; the impact of cluster randomization on the design and analysis of a trial; quantifying the effect of clustering and randomized versus non-randomized comparison. In chapter 2 the authors discuss the historical development of cluster randomization in health research. Chapter 3 addresses issues arising in the planning of CRT such as selecting intervention settings, setting eligibility criteria, and measuring subject response. Most commonly used experimental designs (completely randomized, matched-pair, and stratified) are introduced here and the chapter concludes by presenting strategies for conducting successful trials. Chapter 4 is devoted to the role of informed consent and other ethical issues. Sample size estimation is presented in chapter 5, which is in my opinion, the best-written chapter. Formulae for comparison of means, proportions and incidence rates are presented for the three designs and the chapter ends by presenting strategies for achieving desired power. Chapter 6 is devoted to analysis of binary outcomes on both cluster-level and individual level analyses. Similar analyses for quantitative outcomes are presented in chapter 7. Chapter 8 is devoted to the analysis of count, time to event and categorical data. Cox proportional hazard model is presented here. Reporting outcomes of CRT are addressed in chapter 9.

It is fair to say that the book is well organized and the material covered is suitable for practical use. Although the book is thorough and nearly all aspects CRT are explained clearly, however, I feel that the reader would benefit from more examples to describe the illustrated methods. Another important feature that is missing in this book, is the lack of integration of the software into the text. More information on software and codes to analyze the data are needed. I feel that a chapter on Bayesian methods for analyzing CRT data is needed to complement other methods illustrated in the book.

The serious user of CRT who consults this book will probably find an important discussion of most topics of interest. This book is highly recommended for statisticians, graduate students and researchers designing and analyzing RCT.

ISCB Subcommittees

Please contact the chairs of these subcommittees for further information.

Title	Terms of Reference	Members
Fraud	1. To promote the role of appropriate biostatistical contributions in the assessment of misconduct. 2. To develop statistical tools for assessment of data fabrication and falsification.	**Chair**: **Prof. Emmanuel Lesaffre (B),** **Members**: Dr Marc Buyse (B), Dr Lutz Edler (D), Prof. Stephan Evans (UK), Prof. Stephen L. George (USA), Prof. Gordon Murray (UK), Dr Jonas Ranstam (S), Dr Peter Lachenbruch (USA)
Statistics in Regulatory Affairs	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 absence, the Vice-President. http://www.ucl.ac.uk/~ucaksjs/Guidance.html	**Chair**: Dr Jørgen Seldrup (SGP), **Secretary**: Prof. Stephen Senn (UK), **Members**: Prof. Helmut Schäfer (D), Mr Karsten Schmidt (DK) **Dr Harbajan Chadha-Boreham (CH),** Dr Anna Petroccione (I)
Education	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**: **Prof. Carol Redmond (USA),** **Members**: Prof. Michael Schemper (A), Dr Albert Cobos (E), Prof. Mike Campbell (UK), Dr Shai Linn (ISR)
Student Conference Awards	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**: Prof. John Whitehead (UK), **Secretary**: Mr Bjarne Nielsen (DK), **Members**: Dr Marc Buyse (B), Dr Bruno Cesana (I), Mr Simon Day (UK)
Communications	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 e-mail or the World Wide Web.	**Chair**: **Dr David Warne (CH),** **Secretary**: Mr Bjarne Nielsen (DK), **Members**: Dr Nancy Geller (USA), Dr Elisabeth Svensson (S), Ms Caroline Jackson (UK)
National Groups and other countries with exchange control restrictions or barriers	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 to receive waivers from the annual meeting registration fee and other financial assistance.	**Chair**: Prof. Michael Schemper (A), **Members**: Prof. John Whitehead (UK), Dr Jorgen Seldrup (SGP), Dr Siem Heisterkamp (NL), Prof. Norbert Victor (D), Dr Julia Singer (H), Dr Ewa Kawalec (PL), Dr Elia Biganzoli (I), Mr Simon Day (UK)
Operations	1. To review operations under the constitution and make recommendations (if necessary) for clarifications and amendments. 2. To collate, prepare or initiate preparation of the society's operating procedures.	**Chair**: Mr Karsten Schmidt (DK), **Members**: Mr Simon Day (UK), Dr Tony Johnson (UK), Dr Nancy Geller (USA)

ISCB23 Dijon: 9-13 September 2002

From Stephen Senn and Harbajan Chadha-Boreham

ISCB will be returning to France in 2002 for its 23rd scientific meeting and for the first time since ISCB 11 1990, when the meeting was held in Nimes.

The location is Dijon, capital of Burgundy, formerly a great power in its own right but now a region of France famed for its wine and food. Louis Pasteur was born in nearby Dôle and taught physics in a secondary school in Dijon before being called to an academic career as professor of chemistry at the University of Strasbourg. Roger Guillemin, who shared the 1977 Nobel prize in medicine for the role of the hypothalamus in regulating the pituitary and who discovered the endorphins was born in Dijon and studied at the local university. The Swiss philosopher, Jean Jacques Rousseau wrote his first important work, A Discourse in the Science and the Arts, for the prize of the famous Academy of Dijon.

With its combination of scientific tradition and gastronomic excellence, Dijon will provide, we are confident (well, 99.9% confident) a wonderful venue for all. It will give conference delegates to ISCB 2002 the chance to discover that "pleasures of the table" can mean more than just happy hours perusing Fisher and Yates, calculating measure of association, or even, documenting clinical trial reports! In short, dear reader, when it comes to conference venues, Dijon definitely cuts the mustard.

The members of the Scientific Committee have been toiling in cyberspace under the direction of their less-than-efficient chairman and, despite this crippling handicap, have come up with a programme that should have something for everything. Pre-conference courses will cover, "adaptive and sequential procedures for clinical trials" and "methods for interval censored data" and there will be plenary sessions on clinical trials, genetics, statistical modelling, infectious epidemiology (make sure you catch that one) and causality assessment in observational studies.

As is traditional, the mini-symposium will reflect local interests. The general theme that has been chosen is demography, a field in which France has been pre-eminent. It is intended that this session will concentrate in particular on human fertility. Since what is generally regarded as the first significance test was Arbuthnot's examination of the sex ratio at birth, what could be a more appropriate theme than this for the Society for Clinical Biostatistics to consider?

On that note, and for the benefit of those who regard significance tests as an abomination, and prefer more Bayesian modes of reasoning, let me repeat an old conundrum in probability. "M. Dupont has two children at least one of whom is a boy. What is the probability that the other is a girl?*" Answers on a postcard to the editor please!

In the meantime, on behalf of the Scientific Committee for ISCB 23, I wish you all the best for the coming year. I hope to see as many of you as possible in Dijon.

Stephen Senn, Chairman,
Scientific Programme Committee, ISCB 23 Dijon.

*You are allowed to assume:

1) Which is not quite true, (see Arbuthnot) that the sex ratio at birth is 1:1.
2) Which is not quite true either, that there is no differential mortality of the sexes.
3) Which is also not quite true, that there is no tendency for some men to have boys and others girls.
4) Which is self-evidently true and indisputable, that your correspondent is an honest man who never imparts "side" to any of his remarks and who can be trusted in all matters and that hence M. Dupont is a random, nay typical, Frenchman of the two-children variety.

The Dijon Conference will be held at Palais des Congrès, 9 – 13 September 2002. The Local Organising Committee has been meeting regularly. The Scientific Programme Committee was constituted recently and they have come up with interesting and wide range of topics, as you can see from the lively description by Stephen Senn.

In the spring, I set out along the "Route des Grands Crus" to look at the famous castles standing in ancient vineyards. The vines were beginning to wake up from their winter dormancy and I remembered how wonderfully golden red they turn in the autumn, giving the name "Côte d'Or" to the region, meaning "Golden Hills". I also went along to the centre of Dijon to the Tourist Office, housed in one of Dijon's most exquisite buildings, where one feels that Shakespeare could well have stood and imagined the young Romeo and Juliet meeting in the balcony over the courtyard.

I hope to see you in Dijon for the 23rd ISCB Meeting to participate in the dissemination and advancement of Clinical Biostatistics in a convivial and beautiful setting of ancient and modern Burgundy.

The First Announcement for the Dijon Conference will appear at the Stockholm conference, where you will find more details of the Scientific and Social Programme.

Harbajan Chadha-Boreham (Chair, Local Organising Committee)

Local Organising Committee
Harbajan Chadha-Boreham (Chair)
Catherine Quantin (Co-chair)
Philippe d'Athis (Treasurer)
François-André Allaert (Publicity)
Liliane Dusserre

Scientific Co-ordinators
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Catherine Quantin (Co-chair, LOC)

Scientific Programme Committee
Stephen Senn (Chair)
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Peter Diggle (UK)
Val Federov (USA)
Philip Hougaard (Denmark)
Witold Kupsc (Poland)
Thiery Moreau (France)
Michael Proschan (USA)
Amy Racine (Switzerland)
Helmut Schaefer (Germany)

Book Review by Rolf Holle (Germany)

Quality of Life - Assessment, Analysis and Interpretation,
By Peter M Fayers and David Machin. John Wiley & Sons, Chichester, 2000.

With quality of life (QoL) having become an essential aspect of clinical research, many people will welcome this new book by Peter Fayers and David Machin because it gives an integrated and comprehensive introduction to the psychometric and biostatistical issues of this topic. The authors state in the preface that their aim is to explain the methods and techniques in a non-technical way and to provide a practical guide that covers the wide range of methods which are useful for assessment, analysis and interpretation of QoL research.

The book is about 400 pages long and can be divided into three parts of roughly equal size: the first part deals with measuring QoL, the second is concerned with the analysis, and the third deals with study design and practical issues. The appendix contains 15 examples of generic as well as disease specific QoL questionnaires.

Chapter 1 starts with several motivating examples which show that QoL assessment in randomised clinical trials can provide relevant additional information. As a consequence, one can argue that trialists need to justify if QoL is not used as an endpoint in a clinical trial. Fayers and Machin provide guidance in which situations trials should include QoL as a primary or secondary endpoint. The overview of existing QoL instruments is well structured and with examples of questionnaires printed in the appendix, gives a broad first impression of the concepts of QoL without requiring much theoretical background. In later chapters of the book many of these instruments serve as examples in the illustration of statistical methods.

In chapters 2 to 6 the main focus is on psychometric methods for the construction and evaluation of QoL instruments. Chapter 2 introduces the basic concepts of measurement instruments such as reliability and validity and their different facets. Emphasising on some fundamental concepts, like the distinction between psychometric and clinimetric scales or between indicator and causal variables, helps the reader to understand the psychometric strategies explained in later chapters. In chapter 3 these concepts are explained in more detail and it is here that the outstanding didactic principle of the book, the inclusion of examples to illustrate each method, really pays off. The variety of validity concepts which are used because there is no gold standard criterion for QoL can be better understood than in the classic psychometric textbooks. However, some confusion still remains in this presentation, e.g. when internal consistency as measured by Cronbach´s coefficient a is regarded as an aspect of internal validity as well as of reliability. Also, sensitivity and responsiveness are introduced as distinct concepts although they could be regarded as specific facets of validity.

Chapter 4 is titled “Multi-item scales“ but it starts with an unmotivated introduction to significance tests and correlation methods and goes on to specify some of the concepts introduced in chapter 3, but with emphasis on multi-item scales. The subchapter on internal consistency would have fitted well into the previous chapter. Chapters 5 and 6 are more homogenous and give a very clearly written account of factor analysis and item response theory respectively. As in previous chapters the presentation benefits very much from the extensive practical example which serves to illustrate all important issues of factor analysis. The psychometric part of the book ends with chapter 6 introducing item response theory which may be less familiar to most readers. Again, the authors succeed in explaining the underlying model and its assumptions. Fayers and Machin admit that item response theory may not be suitable for regular use in QoL scale development because the necessary assumptions are too frequently violated, but for those readers who are familiar with basic statistical principles and methods this is one of the most interesting chapters of the book.

Chapter 7 looks at questionnaire development from a practical rather than a theoretical perspective and gives many useful hints. One has to accept that most of them are based on conventional wisdom rather than on mathematical theory or clear empirical evidence.

The following five chapters of the book are concerned with the statistical analysis of QoL data. They are structured in two introductory chapters with basic methods for the cross-sectional and the longitudinal approach and then address specific topics of special importance in QoL analysis. Chapter 8 is basic statistics on 25 pages, but some may wonder whether all of this (e.g. the illustration of histograms and bar charts) is necessary when the authors state in the preface that they “have assumed some familiarity with basic statistical ideas“. Obviously the authors have written a book for a wide spectrum of potential readers and in some places I have wondered whether they should have advised the statistical novice to first read Doug Altman’s “Practical Statistics for Medical Research“ instead of attempting to write an “all-in-one“ book. Nevertheless, many readers will be grateful that Fayers and Machin have chosen the latter approach.

Chapter 9 on longitudinal data analysis is somewhat more specific and has more interesting examples from real QoL studies. Among the illustrated methods are some nice graphical approaches for visual exploration of the data. These examples show the typical problem of having an increasing number of missing data over time and the authors repeatedly point out to the reader the dangers of ignoring informative missing data. However, this remains the central problem in the analysis of QoL because most of the methods presented in the book assume that data are complete or missing data are uninformative. In chapter 10, Fayers and Machin demonstrate how advanced statistical methods including multi-level models and GEE methodology may be used to describe complex data with a small number of parameters for which estimation and test procedures exist. According to their didactic approach they always try to make clear which assumptions are implicit in the models and how results from model based analyses can be interpreted.

The problem of missing data gets due attention in chapter 11, part of which is devoted to a detailed presentation of standard imputation techniques. The scope of the book does not allow more detail, e.g. concerning multiple imputation, but here as well as in other places, the authors give their readers a hint regarding more advanced techniques and further reading. Sceptical readers are informed that not imputing missing data also involves making assumptions and therefore is not a priori the better alternative.

Book Review by Rolf Holle (continued)

The last chapter on analysis of QoL data is headed "Quality-adjusted survival" and gives a short introduction into the utility based QALY concept. In accordance with the authors´ background in clinical trials, the presentation focuses on the Q-TWIST approach and the use of QALYs in health economic studies is only briefly mentioned. This was a wise decision because an adequate treatment of the QALY methodology and its problems would not have fitted into the frame of this book. Here, as in other chapters, readers are advised to read the short summarising conclusion at the end of each chapter where Fayers and Machin express their critical view towards the application of some of the methods presented.

The last part of the book is concerned with practical aspects and clinical interpretation. I found chapter 13 very helpful and essential reading for those who are planning their first clinical trial with QoL assessment, because it shows various organisational measures which may help to minimise missing data. This is no trivial stuff and many researchers only realise what organisational effort and discipline is necessary after their first multi-centre trial results in a QoL data set that is too fragmentary to be analysed. Chapters 14 and 15 are again not very specific to QoL and in the former the standard set of sample size formulae is presented and illustrated with QoL examples. In chapter 15 on practical and reporting issues there is a lot of overlap with previous chapters and I wondered why the authors included subchapter 15.4 "Elements of good graphics" which does not add anything substantial to the presentations given in 8.6 and 9.2. In addition, the problem of multiplicity in statistical testing is addressed on p. 305 and again on p. 311, but in each case only very briefly.

Overall, this book can be highly recommended to a broad range of potential readers. It will be most useful for those who have basic biostatistical knowledge and only little experience with QoL studies. For more advanced readers it still has much to offer because it covers the topic very broadly ranging from psychometric methods to multilevel analysis models. Fayers and Machin are competent in both practical and theoretical issues of QoL research. Their didactic ability and the inclusion of a large number of numeric examples contrasted from the rest of the text help to make the book easy to read. If I could make suggestions for the second edition, I would want a bit more structuring of this all in all well-structured textbook. Summarising the main points of each chapter or subchapter in form of a short checklist would improve the readability. For a book written jointly by two authors the homogeneity of the presentation is remarkable, but there still are some points for improvement where topics are addressed repeatedly in different chapters or the same abbreviation (ICC) has two different meanings.

Book Review by Peter Lachenbruch (USA)

Handbook of Parametric and Nonparametric Statistical Procedures, by David J. Sheshkin, Publisher: CRC (2000)

This book covers an impressively wide range of statistical tests, including all the common ones, and some of the uncommon ones also. Each chapter deals with a single test and is organized in eight sections:

1. Hypothesis Evaluated with Test and Relevant Background Information
2. Example
3. Null versus Alternative Hypotheses
4. Test Computations
5. Interpretation of the Test Results
6. Additional Analytical Procedures for the test and/or related tests
7. Additional Discussion of the Test
8. Additional Examples Illustrating the Test's Use

These are quite useful and will provide many users a handy reference source. I found some shortcomings that have to do with the general approach of the book, the coverage, and the information given.

Although the title includes the word "procedures' the focus in entirely on tests. There is a single paragraph on page 17 that mentions estimation and confidence intervals. This is an area that many of us would like to have in a reference (e.g. how to use nonparametric procedures to get confidence intervals).

The topics are more related to social science than Biostatistics, Medical Statistics or Clinical Trials. Thus, I found nothing on survival analysis methods, exponential or Weibull distributions, log-normal distributions, etc. There is no comment on the Mantel-Haenszel test. Although the Mann-Whitney U statistic is presented, there is no indication that the Wilcoxon rank sum test exists and has a relationship to the Mann-Whitney U. The Wilcoxon signed rank test is discussed. I did not find anything on tests for normality (other than as part of the goodness-of-fit tests). For example, neither the skewness-kurtosis test nor the Shapiro-Wilk test is mentioned. There is no discussion of testing or estimation for Risk Ratios (relative risk) or Odds Ratios.

I would have welcomed some additional information in each section on sample size computation for the tests, how robust each procedure is to violation of assumptions, and what competitors there are for each test. In fairness, there are tables on pages 28-30 providing "Decision Table for Inferential Statistical Tests…" for ordinal/rank-order data, for categorical/ nominal data, and for measures of correlation/ association.

Regarding robustness, the book is lacking much useful information. Typically there is a statement that if "the aforementioned assumptions are saliently violated, the reliability of the z test statistic may be compromised" (p.33). I'd like to know if substantial skewness is worse than heavy tails, the effect of unequal variances when I assume equality, etc. For the Pearson Correlation Coefficient, there is no discussion of the effect of non-normality on the test (it's serious!).

In summary, I find there is a wealth of information for the professional statistician who can go to other sources to fill in gaps, but the Biostatistician has some tests and estimation procedures that are missed.

Books and Software for Review

In this issue:

Author(s)	Title	Publisher (year)	Reviewer
Peter M Fayers and David Machin	Quality of Life: Assessment, Analysis and Interpretation	John Wiley (2000)	Rolf Holle
John Matthews	An Introduction to Randomised Controlled Clinical Trials	Arnold (2000)	Rosa Jimenez
Helen Brown & Robin Prescott	Applied Mixed Models in Medicine	John Wiley (1999)	Paul Johnson
David J Sheskin	Handbook of Parametric and Nonparametric Statistical Procedures	CRC (2000)	Peter Lachenbruch
Peter L Bonate	Analysis of Pretest-Posttest Designs	CRC (2000)	Bruno Cesana
Alistair C Wardlaw	Practical Statistics for Experimental Biologists (2nd ed)	John Wiley (2000)	Ettore Marubini
John Haigh	Taking Chances: Winning with Probability	Oxford (2000)	Carla Rossi
Allen Donner & Neil Klar	Design and Analysis of Cluster Randomisation Trials in Health Research	Arnold (2000)	Sadik Khuder
Sophia Rabe-Hesketh & Brian Everitt	A Handbook of Statistical Analyses Using Stata	CRC (2000)	Piergiorgio Duca

Reviews awaited:

Peter Armitage (ed)	Encyclopedia of Biostatistics: Vol. 4: Med-Pre	John Wiley (1998)	Aurelio Tobias
Donald C Monkhouse & CT Rhodes (Eds.)	Drug Products for Clinical Trials	Marcel Dekker (1998)	Koos Lubsen
Edward L Korn & Barry I Graubard	Analysis of Health Surveys	John Wiley (1999)	Dario Gregori
Chi-Lun Cheng & John W Van Ness	Statistical Regression with Measurement Error	Arnold (1999)	Victor Moreno
Michael R Hamrell (ed)	The Clinical Audit in Pharmaceutical Development	Marcel-Dekker (2000)	Marc Buyse
Shein-Chung Chow & Jen-Pei Liu (1)	Design and Analysis of Bioavailability and Bioequivalence Studies	Marcel-Dekker (2000)	Laszlo Endrenyi
James E. De Muth	Basic Statistics and Pharmaceutical Statistical Applications	Marcel Dekker (1999)	Ann Martin
CF Jeff Wu & Michael Hamada	Experiments: Planning, Analysis, and Parameter Design Optimisation	John Wiley (2000)	Gilg Seeber
Darlene K. Stangl & Donald A. Berry (eds.)	Meta-Analysis in Medicine and Health Policy	Marcel Dekker (2000)	Marc Saez

Reviewers wanted:

Martin Bland	An Introduction to Medical Statistics (3rd ed.)	Oxford (2000)	-
Martin Bland and Janet Peacock	Statistical questions in Evidence Based Medicine	Oxford (2000)	
Douglas G Altman, David Machin, Trevor N Bryant, Martin J Gardner (eds)	Statistics with Confidence (2nd ed.)	BMJ (2000)	
Philip Hougaard	Analysis of Multivariate Survival Data	Springer (2000)	
Joseph L Gastwirth (ed)	Statistical Science in the Courtroom	Springer (2000)	
Terry M Therneau & Patricia M Grambsch	Modeling Survival Data: Extending the Cox Model	Springer (2000)	
Geert Verbeke & Geert Molenberghs	Linear Mixed Models for Longitudinal Data	Springer (2000)	
Mitchell H. Gail & Jacques Benichou	Encyclopedia of Epidemiologic Methods	John Wiley (2000)	
David W. Hosmer & Stanley Lemeshow	Applied Logistic Regression (2nd ed)	John Wiley (2000)	
Andrew B. Lawson	Statistical Methods in Spatial Epidemiology	John Wiley (2001)	
A H Leyland & H Goldstein	Multilevel Modelling of Health Statistics	John Wiley (2001)	
Simon Day	Dictionary for Clinical Trials	John Wiley (1999)	
Alex J Sutton, Keith R Abrams, David R Jones, Trevor A Sheldon & Fujian Song	Methods for Meta-Analysis in Medical Research	John Wiley (2000)	

Yes ! The last 12 books are new and are available for review. Deadline for requests: 31 July 2001.

Arnold:	http://www.arnoldpublishers.com
Chapman & Hall:	http://www.crcpress.com/www/chaphall.htm#ms
John Wiley:	http://catalog.wiley.com/index.cgi?
Marcel Dekker:	http://www.dekker.com/catalog/catalog_top.htm
Oxford:	http://www4.oup.co.uk/
Springer:	http://www.springer.de/statistic/books/newbooks.html

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 e-mail, html, RTF or Word are preferred. I may edit the reviews for clarity (English grammar and spelling, punctuation etc.).

Book Review by Rosa Jimenez (Cuba)

An Introduction to Randomised Controlled Clinical Trials, by J.N.S. Matthews, Arnold (2000)

Clinical Trials have become a sort of protector of human health in the sense that in these days they constitute the main tool to evaluate, quantitatively and rigourously, the benefit and also the security of novel therapeutic means. The leit motiv of this type of research design is methodologic strictness; placed as they are in the dilemma of deciding, from a sample, whether some new therapeutic modality, totally or partially new, contributes or not to the advancement of healing of a disease or any human abnormal condition.

Matthews' book is, as its name suggests, an introductory book, a basic book but with a wide scope focused on the most relevant design among Clinical Trials: Randomized Controlled Clinical Trials (RCT).

Differently from other books about the topic, Matthews' book, in spite of its introductory nature, aims to provide the reader with an acceptable knowledge of the statistical theory underlying the methods discussed here. The author does not restrict himself, as one can observe in other similar textbooks, with a light statistical explanation that appeals mainly to intuition.

Furthermore, the book tends to be exhaustive It includes, at least, a wide compendium of concepts and procedures (old and modern) involved in RCT; from methods and formulae to sample size calculation, to the Bayesian approach for the inference process (which is included as an alternative method for incorporating accumulated data to decisions or Metaanalysis for RCT (treated with an acceptable depth in a whole chapter). Other aspects that could be considered out of the scope of an introductory book are: analysis for equivalence trials and multiple response evaluation. Nevertheless Matthews' book adequately includes these two topics.

A very positive feature of the reference book is the number of examples. The author does his best to find plausible explanations for all the topics he deals with and achieves a good part of this goal through the use of adequate examples, a fact thamakes topics that are normally tough to understand, like Covariance or Subgroup Analysis, become less impenetrable.

The number of exercises at the end of each chapter, (with answers at the end of the book), also adds to the attraction of the book and makes it more useful for those who want to introduce themselves to the problem of assessing and analysing data from RCT and for the students for whom this book is especially intended.

However, purely methodological passages are also available. For instance, the chapters dealing with protocol deviations, definition and description of bias (often poorly treated in other similar books) and treatment allocation, blindness and placebos. This feature makes the book useful also for professionals who might read it from an entirely medical position.

Another characteristic of the book is its clear language. In spite of its expressed intentions (see the preface) of answering purely mathematical questions, the language used makes the book suitable for medical students too.

Regarding the sequence of the topics; the book begins with an introductory chapter that explains the concept of an RCT, its historical position, the need and the justification of the existence of this kind of research, and their more relevant features: the necessity of concurrent controls and randomized allocation. This introductory chapter is followed by four basic methodology chapters: one deals with bias problems and types of bias; one introduces the necessity of a proper sample size and ways to achieve it; one describes different methods of allocating patients to groups; and one explains the concept of blindness, the placebo effect and the use of placebos. Another chapter deals with topics related to data analysis, where aspects like confidence intervals and their meaning; the treatment of baseline data and analysis of covariance are introduced. Two chapters relative to the analysis of data, with more statistical contents, follow: the use of repeated measures (used frequently in RCT where results of treatment are measured through the evolution of the disease), the possibilities of an analysis by subgroups and the issue of multiple responses.

The book ends with a chapter that completes the RCT panorama: the management of unavoidable protocol deviations (where an aspect recently introduced in the methodology of CT, the "analysis by intention-to-treat" and its justification is included).

The author adds two more chapters, that complete his purpose of giving a complete view of RCT and its context: the use of special designs (crossover, equivalence trials and cluster randomised trials) and the chapter devoted to introducing Meta-analysis, its usefulness, justification and principal features.

To summarise, we have a book that deals with the timely theme of CT with a wide scope, a clear language and an express intention that the reader understands the mathematical theory underlying each of the methodological and statistical methods employed in this area.

It has a wide scope but is kept brief because it is fully intended as an introductory book for students who will eventually become specialists in this passionate area of clinical research.

Book Review by Piergiorgio Duca (Italy)

A Handbook of Statistical Analyses using Stata. by Sophia Rabe-Hesketh and Brian Everitt, 2nd edition, CRC (2000)

Starting from the authors' point of view that "Stata is particularly useful for modelling complex data from longitudinal studies or surveys and is, therefore, ideal for analysing results from clinical trials or epidemiological studies", this book contains, in 12 Chapters, many topics of an intermediate-advanced course on biostatistics (Analysis of Variance, Multiple regression, Logistic regression, Longitudinal data analysis, Survival analysis, Principal components analysis), including in the first one what a new user has to know on using Stata 6.

In each chapter the authors illustrate how Stata can be used dealing with a particular data set, frequently taken from "Handbook of small data sets" (1994) by Hand D.J. et al., applying a particular statistical technique.

They always introduce and describe the data (about female psychiatric patients in chapter 2, about determinants of pollution in U.S. cities in chapter 3, about treating hypertension in chapter 4, about treatment of lung cancer and diagnosis of heart attacks in chapter 6, about the treatment of postnatal depression in chapter 8 and so on). They briefly discuss the appropriate analysis for it, including a brief account of the statistical background of the technique applied, extensively referenced.

The authors pay particular attention to model fitting evaluation using graphs, discussing the models' assumptions, suggesting graphical approaches to their validation. Unfortunately the quality of graphs is not always excellent.

Given that the primary focus is on using Stata 6 and interpreting results, the text could be suggested to teachers, as a support for practical in an intermediate or advanced course on Biostatistics, or directly to researchers and students, as a self learning text on doing statistical analyses.

4-6 exercises at the end of each chapter, and the exhaustive answers to selected exercises given in Appendix, give to the reader the opportunity of self evaluating his/her comprehension.

ISCB22 Stockholm: 19-23 August 2001

22nd Annual Meeting
The International Society for Clinical Biostatistics, ISCB
19-23 August 2001, Stockholm, Sweden

On behalf of the Local Organising Committee (LOC) and the Scientific Program Committee (SPC) we warmly wish youwelcome to Stockholm in August! We promise you a varied programme of high quality. The SPC received a large number of abstracts for oral or poster presentations, with an excellent overall scientific level. As a result both the number of contributed paper and poster sessions have been increased.

Besides the traditional focus on statistical methods in clinical medicine and epidemiology, the Stockholm conference puts special emphasis on statistical genetics and statistical methods in bioinformatics, notable the statistical analysis of DNA microarray data.

The topics for the two pre-conference courses are **Event History Analysis** (**Per Kragh Andersen** and **Niels Keiding**, Copenhagen) and **Introduction to Genetic Epidemiology** (**David Balding** and **John Whittaker**, Reading).

The mini-symposium on **Cancer Genetics and Bioinformatics** (**Douglas Easton**, Cambridge) aims at a broad discussion on methodology for identifying genetic determinants for disease and for prognosis and treatment prediction. We hope that the symposium generates discussion among statisticians, clinicians, cancer epidemiologists and molecular geneticists alike.

Your attention should also be drawn to **Stephen Evans'** lecture **on Science, Statistics and Scandal in Drug Safety**, by special invitation of Simon Day, the ISCB President.

The full programme will be continuously updated on the Conference Website www.iscb.stockholm2001.org.

Please, note that the **deadline for registration with reduced fee is June 15.**

Welcome to Stockholm!

Juni Palmgren, LOC Chair
Simon Thompson, SPC Chair

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If you have not received an e-mail from ISCB-egroups, we do not have your correct e-address. Please send it to the editor at 100557.2260@compuserve.com and the ISCB office at iscb@post3.tele.dk. Thanks !

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ISCB21 Stockholm: Draft Programme

From the Stockholm Webpages, 04 June 2001: **TIMETABLE**

	Saturday 18 August	Sunday 19 August	Monday 20 August	Tuesday 21 August	Wednesday 22 August	Thursday 23 August	Friday 24 August	Saturday 25 August	Sunday 26 August
09.00-10.30		Pre-conference courses	Invited Session	Invited Session	Invited Session Contributed Sessions	Mini-symposium			
10.30-11.00		**Coffee**	**Coffee**	**Coffee**	**Coffee**	**Coffee**			
11.00-12.30		Pre-conference courses	Invited Session	Key Note Lecture Annual Meeting	Invited Session Contributed Sessions	Mini-symposium			
12.30-14.00		**Lunch**	**Lunch**	**Lunch**	**Lunch**	**Lunch**			
14.00-15.30		Pre-conference courses	Contributed Sessions	Contributed Sessions	Excursions				
15.30-16.00		**Coffee**	**Coffee**	**Coffee**					
16.00-17.30		Pre-conference courses	Contributed Sessions	Contributed Sessions	Excursions				
18.30			Reception Stockholm City Hall						
19.00				Conference Dinner Vasa Museum					

Poster Sessions: Monday 20, Tuesday 21 and Wedneday 22 August

ISCB Executive Committee Meeting: Sunday 19 August, 18.00+

Pre-Conference Courses: Sunday 19 August 2001

Course 1	Course 2
EVENT HISTORY ANALYSIS Lectures by Per Kragh Andersen and Niels Keiding, Dept. of Biostatistics, University of Copenhagen, Denmark. Based on the monograph "Statistical Models Based on Counting Processes", by P.K.Andersen, Ø.Borgan, R.D.Gill and N.Keiding, Springer-Verlag, 1993. Event history data are obtained by observing individuals over time, focusing on times of occurrence of certain events and the type of event occurring. This course will give a review of event history analysis in continuous time based on multi-state models, starting from the two-state model for survival data and the competing risks and illness-death models. The statistical tools will include non-parametric estimation and testing (the Nelson-Aalen and Kaplan-Meier estimators, the logrank test, survival synthesis, the Aalen-Johansen estimator for transition probabilities in a Markov process), parametric models and models for the transition intensities including covariates along the lines of the Poisson and Cox regression models for survival data. The influence of observational patterns on the inference will be discussed. The exposition will be based on concrete clinical and epidemiological examples from the lecturers' own experience.	INTRODUCTION TO GENETIC EPIDEMIOLOGY Lectures by David Balding and John Whittaker, Dept. of Applied Statistics, University of Reading, UK. The course provides an introduction to the methods used to locate genes contributing to disease and to assess their role. The most basic methods involve studying patterns of disease incidence among families, often extending over several generations, to assess evidence that a disease has a genetic component (segregation analysis). Linkage analysis methods (which can be classified into "parametric" and "non-parametric" methods) involve examinining the genes shared by close relatives to identify the approximate genetic location of genes contributing to a disease. To determine the role of specific genes, we can look for differences in gene frequencies between samples of affected and unaffected individuals, or study the differing patterns of gene transmission from parents to affected and unaffected offspring (association studies). We will introduce each of these approaches. Our emphasis is on the principles of data analysis and study design rather than in the details of particular computational implementations. We will contrast the strengths and weaknesses of the different approaches and try to indicate the circumstances in which each is most appropriate.

ISCB Executive Committee Meeting: Sunday 19 August, 18.00+

Monday 20 August 2001 am

Invited Session 1: 09:00-10:30

I01 Sensitive Analysis for Missing data

I:1 ***Forster Jon*, Smith P.W.F.** : A Model-Based Bayesian Approach to Sensitivity Analysis for Missing Categorical Data
I:2 ***Vansteelandt Stijn* , Goetghebeur E.:** Drawing Inference from a Region of Estimates: Sensitivity Analysis for Missing Data
I:3 ***Rotnitzky Andrea*, Scharfstein D., Robins J.** : Sensitivity Analysis in Follow-Up Clinical Studies with Drop-Out Using Non-Parametric

Invited Session 2: 11:00-12:30

I02 Modelling in Environmental Epidemiology

I:4 ***Donnelly Christl* , Ferguson N., Ghani A., Anderson R.:** Detecting Clusters in a Multidimensional World
I:5 ***Dominici Francesca* , Daniels M., Zeger S.L., Samet J.M.:** National Models for Estimating the Effect of Particulate Matter on Mortality in US Cities
I:6 ***Knorr-Held Leonhard*, Richardson S.:** Space-time Modelling of Infectious Disease Surveillance Data

Monday 20 August 2001 pm (1)

Contributed Sessions 1-4: 14:00-15:30

O01 Sensitive Analysis for Misssing Data

O:1 ***Verzilli Claudio*, Carpenter J.R.**: Assessing Treatment Effect in the Presence of Missing Data: A Computationally Efficient Sampling-Based Sensitivity Analysis

O:2 ***Hutton Jane L*, Hahn S., Williamson P.R.:** Evidence for Outcome Variable Selection Within Studies, and Sensitivity Analyses

O:3 ***Carles Serrat*, Gómez G.**: Estimating the Stratified Survival with Missing Covariates. A Sensitivity Analysis Perspective

O:4 ***Vach Werner*** : On the Predictability of Sensitivity Analyses in the Case of Missing Covariates

O02 Statistical Issues in Clinical Trials

O:5 ***Warn David*, Turner R.M., Thompson S.G.**:Bayesian Hierarchical Modelling of Binary Outcome Data on the Absolute Risk Difference and Relative Risk Scales: Applications to Meta-Analysis and Cluster Randomised Trials

O:6 ***Senn Stephen*:** The Identifiability Problem: Gene by Treatment Interaction, Pharmacogenomics and Cross-Over Trials

O:7 ***Burman Carl-Fredrik*, Hamrén B., Olsson P.:** The Role of Clinical Trial Simulation in Drug Development

O:8 ***White Ian*, Thompson S.:** When Should Skewed Outcome Data in Clinical Trials be Summarised by Their Mean?

O03 Measurement and Misclassification

O:9 ***Rosenfeld Simon*** : Estimating Relative Risk from Data with Strongly Nonnormal Measurement Error

O:10 ***Carstensen Bendix*** : Prediction Between Several Methods of Measurement

O:11 ***Brady Tony* , Royston P :** Putting Patients into Prognostic Groups - Countering Over-Optimism in Prognostic Separation

O:12 ***Sauerbrei Willi* :** On the Necessity of Validation of Classification Schemes with External Data

O04 Genetic Epidemiology and Bioinformatics

O:13 ***Wienke Andreas*, Christensen K., Skytthe A., Yashin A.I.:** A Multivariate Survival Model for Groups of Related Individuals

O:14 ***Plna Kamila*, Lichtenstein P., Hemminki K.**: Environmental and Heritable Causes of Cancer Among 9.6 Million Individuals in the Swedish Family-Cancer Database

O:15 ***Zwinderman Aeilko H*, Maat-Kievit A., Wintrebert C.M.A.**: Frailty Models to Analyze Association of Onset-Age Between Related Individuals with Huntington Disease

O:16 ***Moreno Victor*, Gonzalez J.R.**: Validating Reproducibility of DNA Array Hybridisations

Monday 20 August 2001

Contributed Sessions 5-8: 16:00-17:30

O05 Survival Models for Clustered Data

0:17 *Arends Lidia*, **Stijnen Th.:** Meta-Analysis of Published Survival Curve Data

0:18 *Walker Ann Sarah* , **Babiker A.G.**: Sensitivity of Bivariate Frailty Distributions to Censoring

0:19 *Hemming Karla* , **Shaw J.E.H.:** A Parametric Dynamic Survival Model with Gamma Frailties

0:20 *Xuejun Chen*: A Frailty Model for Clustered Survival Data

O06 Statistical Issues in Clinical Trials

O:21 *Turner Rebecca* , **Omar R.Z., Thompson S.G.**: A Framework for Modelling Multivariate Outcomes in Clustered Data

O:22 *Nixon Richard*, **Thompson S.G.:** Baseline Adjustments for Binary Data in Repeated Cross-Sectional Cluster Randomized Trials

O:23 *Porcher Raphaël* , **Lévyl V., Chevret S**.: Sample Size Correction for Randomized Clinical Trials with Crossovers in Malignant Diseases

O:24 *Bregenzer Thomas*,: Realisation and Interpretation of Nonparametric Point Estimators and Confidence Intervals in Clinical Trials with Multiple Endpoints

O07 Statistical Analysis of DNA Microarray Data I

O:25 *Lee Mei-Ling Ting*, **Whitmore G.A**.: Statistical Methods and Issues in the Analysis of Microarray Gene Expression Studies

O:26 *Heisterkamp Simon*, **Kosters A., Groen B**.: Bayesian Analysis of a Small Scaled Micro-Array Experiment

O:27 *Kropf Siegfrid*, **Eszlinger M.:** Multiple Comparisons in the Analysis of Gene Expression Arrays

O:28 *Mertens Bart J. A.*:Microarrays, Pattern Recognition and Exploratory Data Analysis

O08 Modelling in Environmental Epidemiology

O:29 *Peters Jaime*, **Rushton L., Jones D.R., Abrams K.R., Sutton A.J., Mugglestone M.A.:** Methods for the Synthesis of Epidemiological and Toxicological Research in Environmental Risks to Health

O:30 *Murad S*, **Omar R.Z.:** Issues on Estimating the Effects of Particulate Matter on Respiratory Diseases from a Longitudinal Study

O:31 *Moreno Victor* , **Gonzalez J.R.:** Modelling Cancer Risk Around a Chemical Factory

O:32 *Viboud Cécile*, **Boëlle P-Y., Pakdaman K., Valleron A-j., Flahault A.**: Forecasting the Spatio-Temporal Spread of Influenza Epidemics by the Method of Analogues

Monday 20 August 2001

Poster Sessions 1-7: 08:30-17:30

P01 Statistical Methods in Cost-Effectiveness Studies

P:1 *Pezeshk Hamid* , **Gittins J.**: A Decision Theoretic Approach to Sample Size Question in Clinical Trials

P:2 *Young Tracey*, **Thompson S.G., Buxton M.J**.: The Use of Published Prognostc Scores to Investigate Non-Livertransplant

P:3 *Cooper Nicola* , **Sutton A.J., Mugford M., Abrams K.R.:** Use of Bayesian Markov Chain Monte Carlo Methods to Model Cost-of-Illness Data

P:4 *Norrie John*, **Ford I.**: Modelling Risk & Benefit in Long Term Clinical Trials

P:5 *Sutton Alex*, **Abrams K.R**., Lambert P., Jones D.R.: A Bayesian Approach to Evaluating Net Benefit

P:6 *Hayat Matthew* **Johnson-Masotti A.P., Laud P.W., Hoffmann R., Pinkerton S.D.:** Probabilistic Cost-Effectiveness Analysis of HIV Prevention

P02 Modelling in Environmental Epidemiology

P:7 *Ihorst Gabriele*, **Forster J., Strauch E., Schumacher M., Frischer T., Kuehr J.:** Investigating Medium-Term and Long-Term Effects of Ambient Ozone Exposure on Schoolchildrens Lung Growth

P:8 *Vaittinen Pauli*, **Hemminki K.:** Do Changes in Parity and Maternal Age at First Child Birth Explain the Increasing Trends of Breast Cancer Incidence in Sweden

P:9 *Viboud Cécile*, **Pakdaman K., Boëlle P-Y., Flahault A.**: Statistical Efficiency of Hilbert Transforms for Detecting Synchronization in Epidemiological Time Series

P:10 *Pazdraztytë Rita*, **Braubach M., Bonnefoy X., Zurlyte I., Taraskeviciene I., Krapavickaite D., Sakalauskas L.:** Housing and Health Project in Lithuania

P:11 *Molinari Nicolas*, **Bonaldi C., Daurès J.P**.: Temporal Cluster Detection

P:12 *Li Xinjun*, **Hemminki K., Mutanen P.**: Age-Incidence Relationships in Cervical Cancer Revisited

P03 Missing Data and Measurement Error

P:13 *Stocken Deborah*, **Dunn J.A.:** Results of an Extreme Scenario Sensitivity Analysis for Missing Prognostic Information in a Randomised Pancreatic Cancer Trial

P:14 *Prescott Gordon* , **Garthwaite P.H.:**A Simple Bayesian Analysis of Misclassified Binary Data with a Validation Sub-Study

P:15 *Manor Orly* , **Zucker D**.: Small Sample Inference for the Fixed Effects in the Mixed Linear Model

P:16 *Orre Roland*, **Bate A., Lindquist M., Edwards I.R.**: Recurrent Bayesian Neural Network Applied to Finding Complex Associations in the WHO Database of Adverse Drug Reactions

P04 Phase I or II Clinical Trials

P:17 *Zhou Yinghui*, **Whitehead J.**: Evaluating Bayesian Designs for Phase I Dose-Escalation Studies Using Simulation

P:18 ***Kundt Günther*, Gerber B.** Effects of Adjuvant Tamoxifen on the Endometrium in Postmenopausal Women with Breast Cancer: Statistical Problems of a Prospective Phase II Study Using Transvaginal Ultrasound

P:19 *Billingham Lucinda*, **Stocken D.D., McConkey C.C**.: Randomised Phase II Cancer Clinical Trials: Determining Sample Size

P:20 *Ng Sien-Kiat Paul*, **Palmer C.R.:** Data-Dependent Designs are Needed but Lack of Awareness and Understanding are Preventing their Use in Clinical Trials

P05 Design and Analysis of Equivalence Trials

P:21 *Wang Duolao*, **Täubel J.:** Evaluation of Consistency and Inconsistency Between Average Bioequivalence,
Individual Bioequivalence and Population Bioequivalence: Some Simulation Results

P:22 *Lange Stefan*,: Magnitude and Rationale of Irrelevance Margins in Clinical Equivalence and Non-Inferiority Trials: A Systematic Review

P:23 *Rockette Howard*: Evaluation of Methods for Comparing Modalities for Equivalence Trials in Multireader ROC Studies

P06 Goodness-of-Fit and Validation

P:24 *Pedan Alexander* **:** Overdispersion and Model Diagnostic in Count Data: A Simulation Study

P:25 *Kuss Oliver* **:** Global Goodness-of-Fit Tests in Logistic Regression with Sparse Data

P:26 *Ring Christina*, **Ring A.**: Investigation of the Effectiveness of Regression Methods to Estimate Mean Time and Shape Parameter of Dissolution Processes in Case of Model Miss-Specification

P:27 *Ambler Gareth*, **Omar R., Royston P.:** Validation of Risk Models in Cardiac Surgery

P:28 *Murad S*, **Omar R.Z., Morton L., Taylor K.M**.:Assessing Stability of Risk Models and Their Sensitivity to Missing Data - Examples from Heart Valve Studies

P:29 *Vergouwe Yvonne*, **Steyerberg E.W., Eijkemans M.J.C., Habbema J.D.F.**:Validation of Prognostic Models: From Goodness-of-Fit to Clinical Usefulness

P:30 *Steyerberg Ewout*, **Borsboom G.J.J.M., Eijkemans M.J.C., Habbema J.D.F.:** Validation and Updating of Predictive Logistic Regression Models

P:31 *Lusa Lara*, **Gregori D.:** A Heterogeneity Test for Regression Parameters in Models for Correlated Data

P07 Miscellaneous

P:32 *Gaus Wilhelm*, **Kron M., Högel J.**: General Case Determination Design to Investigate the Efficacy of Primary Prevention Programs

P:33 *Higgins Julian*, **Thompson S.G.:** Presenting Random Effects Meta-Analysis

P:34 *Chen Ruoling*: Measurements of Passive Smoking: Self-Reported Questionnaire or Serum Cotinine

P:35 *Bamias Christina* **White I.R**.: Estimation of the Treatment Effect in Asthma Trials in the Presence of Rescue Medication: Some Approaches and their Limitations

P:36 *Marshall Roger John*, **Fairnie V**.: A Study of Alcohol and Falls in Young People: What Value a Case-Crossover Analysis?

P:37 *Salanti Georgia*, **Ulm K.:** The Use of Multivariate Isotonic Regression in Establishing a Dose-Response Relationship

Tuesday 21 August 2001 am

Invited Session 3: 09:00-10:30

I03 Statistical Methods in Cost-Effectiveness Studies

I:7 ***Briggs Andre,*** **O'Brien B.:**We're Just not Normal: Economists' View on Statistical Methods for Cost-Effectiveness Analysis

I:8 ***O'Hagan Anthony,*** **Chilcott J.B., McCabe C., Oakley J.E., Stevens J.W., Warren E.**: Bayesian Methods in Cost-Effectiveness Analysis

I:9 ***Lin Danyu*****:** Regression Analysis of Incomplete Medical Cost Data

Invited Session 4 - Keynote Lecture: 11:00-12:30

I04 Keynote Lecture by Invitation of the President for ISCB

I:10 ***Evans Stephen,***: Science, Statistics and Scandal in Drug Safety

Tuesday 21 August 2001 pm (1)

Contributed Sessions 9-12: 14:00-15:30

O09 Surrogate Endpoints

O:33 ***Burzykowski Tomasz*** **Buyse M., Molenberghs G.,:** Surrogate Threshold Effect - A New Measure of the Validity of a Surrogate Endpoint

O:34 ***Royston Patrick,*** **Parmar M.K.B.:** Using Intermediate Outcomes to Design Randomised Clinical Trials to Test Many Experimental Treatments Simultaneously

O:35 ***Thiebaut Rodolphe,*** **Jacqmin-Gadda H., Chêne G., Leport C., Commenges D.**:Bivariate Longitudinal Analysis of the Evolution of HIV RNA and CD4 Cell Count in HIV Infection Taking into Account Left Censoring of HIV RNA Measures

O:36 ***Renard Didier*** **Geys H., Molenberghs G., Burzykowski T., BuyseM.**: Validation of a Longitudinally Measured Surrogate Marker for a Time-Event Endpoint

O10 Survival Analysis

O:37 ***Quantin Catherine,*** **Bolard P., Esteve J., Binquet C., Faivre J., Abrahamowicz M.:** Modelling Time Dependent Hazard Rations in Relative Survival: Application to Colon Cancer

O:38 ***Berger Ursula,*** **Kauermann G.**: A Smooth Goodness of Fit Test for Survival Data

O:39 ***Clark Taane,*** **Altman D.G., De Stavola B.:** Quantifying the Completeness of Survival Data

O:40 ***Smits Jacqueline,*** **van Houwelingen Hans C.**: Evaluation of the renal transplant waiting list. An example of a survival analysis on complex data.

O11 Genetic Association Models

O:41 ***Kilpikari Riika,*** **Sillanpää M.J.**: Bayesian Association Mapping in Structured Populations

O:42 ***Ripatti Samuli,*** **Pitkäniemi J., Sillanpää J.**:Joint Modeling of Genetic Association and Population Stratification Using Latent Class Models

O:43 ***Tanck Michael W.T.,*** **Jukema J.W., Klerkx A.H.E.M., Kastelein J.J.P., de Knijff P., Zwinderman A.H.**:Estimation of Multilocus Haplotype Effects Using Weighted Penalised Log-Likelihood

O:44 ***Lange Christoph,*** **Laird N.M., Silverman E.**:An Approach to Unification of "TDT"-Tests: A New Class of Generalized TDT-Tests, its Asymptotic Distribution and Power

O12 Phase I and II Trials

O:45 ***Geller Nancy***: Design of Early Trials in Stem Cell Transplantation

O:46 ***Zohar Sarah,*** **Chevret S.**:Phase I and II Dose-Ranging Clinical Trials: Proposal of a Two-Stage Bayesian Design

O:47 ***Tan Say-Beng,*** **Machin D.**:Bayesian Two-Stage Designs for Phase II Clinical Trials

O:48 ***Chanter Dennis***: The Design and Analysis of Early Phase Studies for Possible QT Prolongation Effects

Tuesday 21 August 2001 pm (2)

Contributed Sessions 13-16: 16:00-17:30

O13 Design and Analysis of Equivalence Trials

O:49 ***Senn Stephen*, D'Angelo G., Potvin D.:** Carry-Over in Three-Treatment, Three-Period Cross-Over Designs With Particular Application To Bioequivalence

O:50 ***Garrett Andrew:*** Therapeutic Equivalence: Fallacies and Falsification

O:51 ***Brannath Werner*, Bauer P., Maurer W., Posch M.**: Sequential Designs for Simultaneously Testing Noninferiority and Superiority

O:52 ***Skipka Guido***: Unconditional Exact Tests to Show Non-Inferiority in Case of Independent Binominal Proportions

O14 Biologic/Genetic Markers and Prognosis

O:53 ***Begun Alexander*, Yashin A., Iachine I.**:Usage of Genetic Markers Data in Longevity Studies of Twins

O:54 ***Lausen Berthold***: On Prognostic Modelling with Gene Expression Data

O:55 ***Riley Richard*, Abrams K.R., Sutton A.J., Lambert P.C., Jones D.R., Burchill S., Heney D.**: Meta-Analysis of Prognostic Tumour Marker Data

O:56 ***Moerkerke Beatrijs*, Goetghebeur E.**: *The Statistical Selection of Genetic Markers*

O15 Statistical Methods in Cost Effectiveness

O:57 ***Abrams Keith*, Cooper N.J., Sutton A.J.**:Identifying for Which Patients an Intervention is Cost-Effective: A Bayesian Approach to Subgroup Analyses

O:58 ***Cooper Nicola*, Abrams K.R., Sutton A.J., Turner D., Lambert P.**: Use of Bayesian Methods for Markov Modelling in Cost-Effectiveness Analysis: An Application to Taxane Use in Advanced Breast Cancer

O:59 ***Billingham Lucinda*, Burton A., Bryan S., Bathers S., Cullen M.:** An Exploration of Alternative Approaches for Analysing Incomplete Cost Data: The Case of Chemotherapy Versus Palliative Care in Advanced Non-Small Cell Lung Cancer

O:60 ***Gorlia T*, Crott R., Neymark N.**: Assessing the Impact of Uncertainty by Using Bootstrap Techniques when Cost and Outcomes Data are Censored: A Case Study of Chemotherapy in Advanced Ovarian Cancer

O16 Statistical Analysis of DNA Microarray Data II

O:61 ***Mansmann Ulrich***: An Extended Full Bayesian Version of the Gamma-Gamma-Binomial Model for DNA Microarray Data which Includes Prognostic Patient Information

O:62 ***Man Michael*, Johnson K., Liao B., Potter D.**:Evaluating Methods for Classifying Microarray Data

O:63 ***Parmigiani Giovanni***: Screening Genes for Expression-Based Molecular Classification

O:64 ***Segal Mark:*** Regression with Expression: Association Approaches for Microarray Data

Tuesday 21 August 2001

Poster Sessions 8-11: 08:30-17:30

P08 Multivariate Survival Models

P:38 ***Barceló Maria Antònia*, Saez M.**: A Modification of the EM Algorithm to Estimate an Andersen-Gill Gamma Frailty Model for Multivariate Failure Time Data

P:39 ***Smith Karen:*** Survival Analysis with Occasionally Observed Covariates

P:40 ***Wintrebert C.M.A*,. Zwinderman A.H.**: Effect-Effect on Survival After Chronic Myloid Leukemia Transplantation: Application of a Time-Dependent Frailty Model

P:41 ***Newell John*, Aitchison T., Kay J.**: The Presentation and Analysis of Bivariate Survival Studies

P:42 ***Novikov Ilya*, Sadetzki S., Freedman L.**: The Comparison of 'Crude' Survival in Several Groups in Competing Risk Model

P:43 ***Oskrochi Reza* Crouchley R., Davies R.B.**: A Multivariate Frailty Model Applied to Brest Cancer Recurrence

P:44 ***Mansmann Ulrich***: A MCMC Method to Handle Interval Censored Clustered Event Data

P:45 ***Ghilagaber Gebrenegus***: Equivalencies and Inconsistencies Between Hazard- and Logistic-Regression in the Analysis of Survival Data with Multiple Causes of Failure

P:46 ***Putcha Venkata***: Random Litter Size Procedures for Developing Exposure-Response Studies

P:47 ***Gregori Dario*, Lusa L., Di Lenarda A., Salvatore L.**: Actual Treatment and Intention to Treat Evaluation of Efficacy of Betablockers and Aceinhibitors: A Marginal Estimating Equations Approach

P:48 ***Galimberti Stefania*, Valsecchi M.G.**: A Permutation Test for the Comparison of Survival Curves for Matched Data

P:49 ***Di Mascio Claudio*, Ballone E., Colagrande V., Nanni Nanni G., Di Nicola M., Di Mascio R.**: Probability of Nephropathy in a Cohort of Diabetic Patients with Retinopathy

P09 Life Course Modelling

P:50 ***Reilly Marie*, Lawlor E.**: Estimating Risk Profile over Time from Stored Blood Samples and Exposure Records of a Case Series

P:51 ***Sund Reijo***: Data Mining in the Event History Framework

P:52 ***Danardono Danardono*, Broström G., Stenlund H** : Multistate Life History of Child Survival Surveillance Data

P:53 ***McCormack Valerie*, De Stavola B.L., dos Santos Silva I., Leon D., Mann V.**: A Comparison of Traditional Statistical Methods and Latent Factors Models to Investigate Possible Associations Between Fetal Environment and Breast Cancer Risk

P:54 ***Gigli Anna***: Completeness Index for the Estimation of Cancer Prevalence

P:55 ***Le Strat Yann*, Bossard N., Plu-Bureau G., Lê M., Estève J., Thalabard J.C.**: Estimating the Effect of Menopausal Status on Breast Cancer Risk in Presence of Both Extrinsic and Intrinsic Uncertainties on Age at Menopause: A Simulation Study

P10 Statistical Issues in Clinical Trials

P:56 ***Leton Emilio*, Pedromingo A.**:Sĩnergy: A New Software for Meta-Analysis

P:57 ***Kundt Günther***: Choice of Values of Parameters for Restricted Randomization Rules

P:58 ***Ring Christina:*** A Common Structure in Metabolite Transit Time Distributions of Different Organ Models

P:59 ***Ukoumunne Obioha***: A Comparison of Methods for Assigning Confidence Intervals to the Intraclass Correlation Coefficient: Application to Unbalanced Data from Cluster Randomised Trials

P:60 ***Hager Corinne*, van't Hof M.A.:** P-Best: In-Between Randomization and Minimization

P:61 ***Gould A. Lawrence***:A Triage Approach to the Analysis of Safety Data from Clinical Trials

P:62 ***Kehl Victoria*, Ulm K.:** Identification of Responders and Non-Responders in Clinical Trials Using the "Bump Hunting" Procedure

P:63 ***MacLennan Graeme*, Thomas R.E., Grimshaw J.M.**:Unit of Analysis Errors in Cluster Randomised Trials to Evaluate the Effectiveness of the Introduction of Clinical Guidelines into Medical Practice

P:64 ***Schouten Hubert***: Linear Regression Analysis of Cross-Over Trials

P:65 ***Kpozehouen Alphonse*, Commenges D., Chêne G., Anglaret X., Dupuis J., Salamon R.**: Using Bayesian Approach to Stop Clinical Trials: DITRAME (Dimunition de la Transmission du VIH de la Mère l'Enfant) Case

P:66 ***Omar R.Z*, Turner R.M., Thompson S.G.**:Effect of Number and Size of Clusters on Estimation of the Between Cluster Variance

P:67 ***Hutton Jane Luise***: Cluster Randomised Trials and Implementation Research: The Ethical Issues

P11 Miscellaneous

P:68 ***Cheung Yin Bun*, Chowbay B., Tan S.B.**:A Hurdle Model of Tumor Recurrences

P:69 ***Haber Michael*, Barnhart H.X.**:New Methods for the Evaluation of Observer Agreement

P:70 ***Vargha Peter:***More than One Disease Categories: Where to Cut

P:71 ***Lambert Paul*, Sutton A.J., Abrams K.J., Jones D.R.**: Comparison of the Use of Study-Level Summary Covariates in Meta-Regression with Individual Patient Data Meta-Analysis

P:72 ***Murad S*, Omar R.Z.**: Hierarchical Models for Left Truncated Repeated Measurement Data

P:73 ***Ramsay Craig*, Grilli R., Grimshaw J.M.**: Meta-Analysis of Interrupted Time Series Designs: What is the Effect Size?

P:74 ***Kates Ronald*, Harbeck N.**: Modelling of Competing Risks in Survival Data Using Neural Networks

P:75 ***Roberts Chris***: Estimates of Precision for Multi-Rater Kappa Coefficients in Inter-Observer Reliability Studies

Wednesday 22 August 2001 am (1)

Invited Session 5: 09:00-10:30

I05 Statistical Analysis of DNA Micro-array data

I:11 ***Dudoit Sandrine*:** Identifying Differentially Expressed Genes in Microarray Experiments

I:12 ***Newton Michael** A:* Hierarchical Models for Gene Expression Data Analysis

I:13 ***Eilers Paul**:* Classification of Microarrays with Penalized Logistic Regression

Contributed Sessions 17-19: 09:00-10:30

O17 Life Course Modelling

O:65 ***De Stavola Bianca Lucia*, Mann V., Hardy R., McCormack V., dos Santos Silva I., Kuh D., Wadsworth M.:** Life-Course Modelling of Birthweight, Childhood Growth and Breast Cancer Risk

O:66 ***Hardy Rebecca*, Morton S., Kuh D., De Stavola B.L., Wadsworth M.:** Testing the Fetal Origins Hypothesis: Is it Prenatal or Postnatal Growth that is Associated with Later Health?

O:67 ***Gray Linsay*, Cortina-Borja M., Newell M.L.:** A Fractional Polynomial Mixed Effects Model for Repeated Viral Load Measurements of HIV-Infected Children

O:68 ***Shkedy Ziv*, Aerts M., Molenberghs G.**: An Hierarchical Bayesian Changepoint Model for Age-Dependent Probability to Become Hepatitits B Carrier

O18 Survival Anlanysis; Alternatives to Hazard Models

O:69 ***van Putten Wim***: A Comparison of Proportional Hazard Models with Mixture Models

O:70 ***Kwong Pui Sze*, Hutton J.L.**: Accelerated Life Models and Components of Variance for Survival Data

O:71 ***Vaida Florin*** : Accellerated Failure Time Models with Random Effects for Clustered Survival Data

O:72 ***Parrinello Giovanni*, Girelli A., Decarli A.**: Analysis of Incipient Diabetic Nephropathy in Type II Diabetes Mellitus Patients Through the Application of a Parametric Model for Survival Data with Competing Risks

O19 Clinical and Vaccine Trial Methodology

O:73 ***Farrington Paddy*, Kanaan M.**: The Estimation of Waning Vaccine Efficacy

O:74 ***Sinha Debajyoti*:** Bayesian Methods for Joint Modelling of Longitudinal and Survival Data With Application to Cancer Vaccine Study

O:75 ***Alahmed Mohammed*, Ahmad R.**: A Group Sequential Method for Monitoring Multi-Armed Clinical Trials

O:76 ***Whitehead John*** On Frequentist Stopping Rules and Bayesian Priors

Wednesday 22 August 2001 am (2)

Invited Session 6: 11:00-12:30

I06 Phase II Clinical Trials

I:14 **M*ariani Luigi*:** Phase II Trials: A Review of Current Methods and Future Challenges

I:15 ***Hanfelt John*:** Variations on Simon's Optimal Design for Phase II Trials

I:16 ***Stallard Nigel:*** Decision Theoretic Designs for Phase II Clinical Trials in Oncology

Contributed Sessions 20-22: 11:00-12:30

O20 Multivariate Survival Analysis; Case Studies

O:77 ***Hougaard Philip* , Gall M-A.:** Development of Microalbuminuria for Patients with Type II Diabetes: A Case Story of Interval Censoring

O:78 ***Ljørring Christian*, Hougaard P.**How Frailty Models Apply to the Analysis of Bleeding Patterns

O:79 ***Lombard Carl***: Using a Correlated Survival Model for Inference on the Gateway Hypothesis in Substance Abuse

O:80 ***Bogaerts Kris*, Leroy R., Lesaffre E., Declerck D:** Modeling Tooth Emergence Based on Multivariate Interval Censored Data

O21 Prediction

O:81 ***Geskus Ronald:*** Predicition of Residual Time to Aids Based on Marker Values

O:82 ***de Bruijne Mark*, van Houwelingen H.**: Survival Prediction with Time-Dependent Covariates: A Simulation Study to Explore Different Prediction Strategies and the Impact of Missing Data

O:83 ***Schemper Michael:*** Predicitive Accuracy and Explained Variation

O:84 ***Clark Taan*, Altman D.G.**: Developing a Prognostic Model in the Presence of Missing Data: A Case Study

O22 Casual Inference

O:85 ***Loeys Tom*, Goetghebeur E.**: Causal Inference with Survival Data in a Proportional Hazards Framework

O:86 ***Salter Amy*** A Graphical Chain Model Approach for Survival Data: Retention on the South Australian Methadone Program

O:87 ***Raab Gillian:*** Is Causal Inference Possible from Cross-Sectional Data?

O:88 ***Fischer Krista*, Goetghebeur E.**: Explaining Causal and Selective Associations in the Presence of Noncompliance in Placebo-Controlled Clinical Trials

Wednesday 22 August 2001

Poster Sessions 12-15: 08:40-14:00

P12 Pharmacokinetics

P:76 *Kundt Günther*, **Wacke R.**: Comparison of Several Approaches of Therapeutic Drug Monitoring Based on Individual Pharmacokinetics

P:77 *Ring Arne*, Weiss M.: Efficiency of Estimators Used in Nonlinear Regression Analysis and Model Selection in Pharmacokinetics

P:78 ***Siersma Volkert*, Mennel C., Sørensen T., Ødum N., Geisler C.T:** Cell Receptor Cycling: Modelling and Estimation

P:79 ***Retout Sylvie*, Mentre F.**: Optimal Designs in Non Linear Mixed Effects Models: Application in Population Pharmacocinetics

P13 Repeated Measures

P:80 ***Pisarev Heti*, Fischer K., Goetghebeur E.** Structural Nested Mean Models in a Repeated Measures Setting

P:81 ***Fidler Vaclav:*** The Variability of Height Measurements in Adults

P:82 ***Stanuch Helena*, Brzostek T.,Pajdak W.,Radwan J.,Zaczek M., Szymczyk B., Hanczakowski , Bochenski J., Szczeklik A., Góralczyk W.**: Analysis of Repeated Measures of the Thrombin Generation in Different Groups of Rats

P:83 ***MacKenzie Gilbert* Pan J.**: Modelling Joint Mean-Covariance Responses in Longitudinal RCTS

P:84 ***Gorkiewicz Maciej:*** Joint Non-Parametric Linearisation of Repeated Measures

P14 Prediction/Classification

P:85 *Royston Patrick*, Parmar M.K.B.: Goodness of Fit in Survival Analysis: Proportional Hazards and Beyond

P:86 ***Lausen Berthold*, Hothorn T., Nguyen N., Peters A., Mardin C.Y.**: Prognostic Modelling and Classification of Glaucoma Patients

P:87 ***Muche Rainer* , Rösch M., Osthus H., Ring C.:** Modeling the Prediction of Return to Work in Patients Suffering from Musculoskelel Disorders Directly and 1-2 Years After Inpatient Rehabilitation

P:88 ***Ambler Gareth*, Brady T. Royston P:** Simplifying Prognostic Models

P:89 ***Mercier Francois*, Rattier S.**: Characterising Effects of Fenofibrate on Lipids and Lipoproteins Using Discriminant Analysis

P:90 *Jäger Bernd*, Wodny M., Biebler K-E., Rudolph P.E.,Below E: Cluster Analysis with Mixed Binary and Metric Data

P:91 ***Cwiklinska-Jurkowska Malgorzata:*** Comparison of Discriminant Methods with Classification Trees on the Basis of a Medical Problem

P15 Miscellaneous

P:92 ***Lambert Paul*, Sutton A.J., Burton P.R., Abrams K.R., Jones D.R.**: How Vague is Vague?

P:93 ***Shcherbatyy Mykhaylo*, Ivankiv K.S.**: Modelling and Optimization of Infectious Disease Processes Based on Delay Differential Equations

P:94 ***Murad Havi*, Lavon A., Sadetzki S., Geyer O., Freedman L.:** Using Ordinal Logistic Regression to Investigate the Relationship Between Physical Activity and Prognosis of Glaucoma

P:95 ***Ramsay Craig*, Matowe L., Grilli R., Grimshaw J.M.:** Misuses of Interrupted Time Series Designs in Implementation Research

P:96 ***Juneau Paul*:** The Analysis of Data from Electroencephalography (EEG) Studies

P:97 ***Kupsc Witold*, Wagrowska H.:** Some Examples of Analyzing Ratios in Epidemiological Study

P:98 ***Wodny Michael*:** Some Relationships Between Smoothing Cubic and Quadratic Splines

P:99 ***Reiczigel Jenö:*** Confidence Intervals for the Binomial Parameter: New Considerations

P:100 ***Stanisz-Wallis Krystyna*, Martyniak J., Kwasniak M.**: The Comparison of Four Methods for Coronary Artery Disease (CAD) Prediction

P:101 ***Dawidowicz Antoni Leon*, Stanuch H., Kawalec E.:** Beta-Regression

P:102 ***Abrahamowicz Michal*, Krewski D., du Berger R.:** Flexible Modelling of the Impact of Long-Term Exposure to Air Pollution: Non-Linear Effects and Non-Proportional Hazards

P:103 ***Baksh Fazil:*** Design Considerations in the Sequential Analysis of Matched Case-Control Data

Thursday 23 August 2001 am

Mini-Symposium on Cancer Genetics: 09:00-12:30

Invited speakers at this half-day Mini-Symposium on Cancer Genetics and Bioinformatics are **Douglas Easton** (CRC Genetic Epidemiology Unit, University of Cambridge, UK), **Christopher Amos** (Dept of Epidemiology and Biomathematics, M.D. Anderson Cancer Centre, University of Texas, Houston, USA), **Timothy Bishop** (Imperial Cancer Research Fund, University of Leeds, UK), **Peter Sasieni** (Imperial Cancer Research Fund, London, UK) and **Kevin Coombes** (Bioinformatics Group, M.D. Anderson Cancer Centre, University of Texas, Houston, USA). The symposium will be led by Douglas Easton, and local cancer researchers will be invited to take part in the discussions.

Book Review by Paul Johnson (USA)

Applied Mixed Models in Medicine, by Helen Brown and Robin Prescott, John Wiley (1999)

Brown and Prescott have written a book that provides an understanding of mixed models. The title suggests "in Medicine", but the methods examined and developed within the book apply equally to other areas of research. The book will be of interest to many.

The application of mixed models is gaining importance in the statistical analysis of research data. The areas of research include medicine, biostatistics, psychology, biology, environmental science, ecology, sociology, pharmaceutical applications and others. There are many interesting examples presented throughout the book. These primarily relate to the medical field. The authors state in the Preface that they wish to "provide the reader with a thorough understanding of the concepts of mixed models". They have been most successful in this purpose. The material in the book is clear and concise. I found the book extremely interesting and thorough. It was most enjoyable to read. The authors use matrix algebra to describe the mixed model and use SAS to carry out example analyses. The SAS procedure, PROC MIXED is often used. The SAS code and outputs are continually listed throughout the book. The book provides for excellent reading throughout its nine chapters.

Chapter 1 provides an introduction to mixed models. Two illustrative examples used in this chapter are an introductory example of a simple cross-over trial and an example of a more complex multi-centre hypertension trial. The authors ask and answer the following questions: "What is a mixed model?" and "Why use the mixed model?" Definitions are provided. Measurements made repeatedly on the same patients are considered. These are identified as repeated measures.

Chapter 2 defines the mixed model with normally distributed errors. Matrix algebra is used in this definition and subsequent formulation. The notation is clear and an example is given for the multi-centre trial of two treatments for the purpose of lowering blood pressure. Numerical methods for fitting mixed models are developed. These include the methods of maximum likelihood, residual maximum likelihood and iterative generalized least squares. Fixed effects, random effects and variance parameters are estimated. Significance tests are carried out. The Bayesian approach to fitting a mixed model is described. This includes specifying a non-informative prior, determining the posterior density and calculating exact probability intervals for the model parameters.

Chapter 3 introduces the generalized linear mixed model (GLMM) for non-normal data. GLMM is an extension of the fixed effects general linear model (GLM) to include random effects, random coefficients and covariance patterns. The authors use matrix algebra for the mixed model representation. The model is fitted using the SAS procedure, PROC GENMOD. Example SAS code and outputs are listed. Generalized estimating equations (GEE) are introduced. The multi-centre trial of treatments example for lowering blood pressure is used to illustrate the methods.

Chapter 4 examines the use of mixed models for categorical data. The fixed effects ordinal logistic regression and the mixed ordinal logistic regression models are described. Matrix algebra is used. The authors consider mixed models for unordered categorical data. A detailed example of an adverse event is given. SAS code and outputs are listed.

Chapter 5 covers multi-centre trial analysis and meta-analysis. The use of a mixed model allows for any additional variation in treatment effects occurring between centres or between trials. An example is provided and SAS code/output listed. Results from several clinical trials are combined to form a meta-analysis.

Chapter 6 covers the topic of repeated measures. The covariance pattern of the repeated measurements is determined and taken into account. Measures of model adequacy and statistical comparisons between models are presented. An example is given for determining the covariate pattern models for normal data. An example is given for count data and residual plots are produced. The random coefficient model is discussed. The sample size is determined for normal and non-normal data for repeated measures.

Chapter 7 discusses cross-over trials. The advantages for using mixed models in cross-over trials are listed. An example of the 'AB/BA' cross-over trial is used for illustration. It involves the comparison of two diuretics in the treatment of mild to moderate heart failure. Higher order complete block designs, including a four-period/four treatment cross-over trial, are considered. Optimal designs are examined and the authors give an example of Balaam's design.

Chapter 8 considers other applications for mixed models. Included are those for repeated measures when taken within the visit of a trial. The authors discuss the use of repeated measures for multi-centre and multi-centre cross-over trials. An example for a matched case control study is provided. The authors estimate variance components in an animal physiology trial. One hundred breaths were measured on four rabbits on each of four days. SAS code and outputs are listed.

Chapter 9 reviews mixed model software. The authors suggest that the most versatile software available for fitting mixed models to normal data is the PROC MIXED procedure in SAS (developed by SAS Institute Inc., Cary, North Carolina). Other software packages are examined. Contact information is given, primarily through web addresses. One example is the software package called BUGS. This is a Bayesian software package that uses the Gibbs sampler and is developed by the Medical Research Council Biostatistics Unit in Cambridge, UK.

The book makes an important contribution to the field. The book contains much useful reference material and is well written. The chapters are threaded together in such a way as to form a well-defined and clear tapestry for the use of mixed models. This book is well suited as a textbook for a course on mixed models. I highly recommend this book to everyone interested in mixed models. It makes a worthwhile addition to a statistical library.

ISCB21 Scientist Conference Awards 2001

From Michael Schemper

The following 10 scientists are being funded by the Society to attend ISCB Stockholm. The Scientists Awards cover free registration, a free course of the choice of the award winner and inexpensive accommodation. The names of the award-winners are:

Gorkiewicz	PL	Maciej Gorkiewicz <mygorkie@cyf-kr.edu.pl>
Reiczigel	H	Jeno Reiczigel <jreiczig@univet.hu>
Pisarev	EST	Heti Pisarev <heti@math.ut.ee>
Fischer	EST	Krista Fischer <Krista.Fischer@rug.ac.be>
Stanuch	PL	mystanuc@cyf-kr.edu.pl
Chen	China	"Ruoling Chen" <r.chen@dundee.ac.uk>
Vargha	H	"Vargha Peter" <VARPET@bel1.sote.hu>
Shcherbatyy	UA	Shcherbatyy <shcherb@franko.lviv.ua>
Dawidowicz	PL	"piotr" <wadowic@kki.net.pl>
Jurkowska	PL	Piotr Jurkowski <jurkomal@mail.atr.bydgoszcz.pl>

Book Review by Carla Rossi (Italy)

Taking chances: Winning with probability, by J. Haigh, Oxford University Press (1999)

"The book is aimed at the 'layman', interpreted as someone untrained in science or mathematics, but wishing to reason probabilistically with confidence", the author says in the Preface, thus the symbols and mathematical expressions are kept to the minimum in the main text. Five appendices present more mathematical developments addressed at readers more familiar with maths. In some places within the main text some material is presented in a box. These boxes are usually more mathematical than the rest and can be ignored without missing the meaning of the main story. Some chapters end with a few exercises aimed at allowing self-evaluation. Solutions are presented later in the text. The book is organized in 13 chapters and 5 appendices. The order of the chapters is mostly unimportant except for Chapter 1 which should be read first and Chapter 13 last, Chapter 6 which should be read before Chapter 10 and Chapter 8 which should be read before Chapter 12.

Chapter 1 presents the basic concepts related to probability using motivating examples from everyday life and historical games and paradoxes. Chapters 2, 3, 4 and 5 contain further developments, all dealt with in a "problem-solving framework" based on various games, either classical (dice, coins, lotteries) or different (football, other kinds of betting or decision problems). The focus is constantly on highlighting paradoxes, counterintuitive issues and common superstitions.

Chapter 2 on Lotteries ends with the following sentence: 'There is no evidence pointing to any single numbers, or combinations of numbers, that are more or less likely to be drawn by the Lottery machine than others. On the other hand, if some numbers did have a greater chance of selection, that might well take many years to become apparent'. Chapter 6 deals with 'Games with few choices' showing how some modelling problems are equivalent to this general scheme from a mathematical point of view. In the summary at the end of the chapter you can read: "Many problems can be set up as 'games with few choices'. Some are obvious ones that arise naturally as games … and the table of payoff can easily be written down. Others, including social conflicts… need some thought in allocating suitable payoff, and the two players may have very different ideas of what these should be".

In Chapter 7 the problem of modelling waiting times is addressed on the basis of some nice and classical examples (birthday or secretary problem). Chapter 8 and 9 deal with further classical and popular games always presented by a friendly but still rigorous approach. Chapter 10 presents classical Casino games such as Roulette, Baccarat Chemin de fer etc., whereas Chapter 11 presents problems arising with betting in horse race, cricket etc. Chapter 12 continues dealing with problems from various sports such as soccer, tennis, golf etc. Finally, Chapter 13 deals with several other problems of various kinds presented as "miscellanea".

In conclusion the book is an excellent presentation of basic probability by means of several interesting examples and problems coming from various games, always the analogies with other issues related to modelling and decision-making under uncertainty are stressed. The book can also be a powerful additional tool for an undergraduate course in probability.

Book Review by Ettore Marubini (Italy)

Practical statistics for experimental biologists (2nd edition), by Alistair Wardlaw, John Wiley (2000)

As stated by the Author in the Preface, the book: "… assumes the reader wants to use statistics in a responsible way, but has little interest in processing data with formulae and a pocket calculator. It is, therefore, for those who want to go onto the computer screen straightaway and become familiar with the statistical methods that can be used there – and the basic ideas behind them." MINITAB is the package of reference.

The subject-matter is subdivided in nine chapters, the first five of which introduce statistical methods suitable for processing continuous quantitative data; namely: 1. A simple experiment in pipetting; 2. How to condense the bulkiness of data, 3. Are those differences significant?, 4. More about measurement differences, 5. Awkward-measurement data. Statistical tools to deal with discrete data are faced in two chapters: 6. How to deal with count data and 7. How to deal with proportion data. Chapter 8 is devoted to Correlation and regression. Dose-response lines and assays are the content of the last chapter.

A common sense approach is adopted to introduce the rationale of the statistical tools of current use in a biological laboratory; for each of the latter, the pertinent instructions to process the data by MINITAB are given in detail. Resorting to the "altered data sets" appears to be a noticeable device from a didactical viewpoint; the "Further notes" appear to be extremely helpful for a thorough comprehension of important statistical concepts. Thus the book can be profitably adopted as a reference manual in a course of Introduction to Statistics for biologists.

However, the following considerations seem pertinent: i) as the paramount importance of the interaction concept for a biologist, a wider and deeper discussion than that given in 4.3.2 (meaning of interaction) would be appreciated; ii) table 9.8 reports the sample result of an experiment carried out according to a randomised block design. The corresponding ANOVA would enable the researcher to test directly the "Plate" effect by the test F= = 2.85 (P = 0.097) with 3 and 9 d.f. respectively; iii) page 218: "P = 0.000 for Prep. Means….." A note in line with Finney (Statistical Method in Biological Assay, Charles Griffin, 1964, page 108) could be welcome. iv) page 55, line 35-36: MS has to be read SS; v) page 216, figure 9.7: all points are reported in solid squares so that Standard and Unknown cannot be distinguished.

ISCB21 Student Conference Awards 2001

From John Whitehead

The following 5 students are being funded by the Society to attend ISCB Stockholm. We had 9 entries and the standard was high. Those who did not win should not be discouraged, as the scoring was very close. The Subcommittee is keen to see a greater number of entries in future years.

Fazil Baksh
Department of Applied Statistics, University of Reading, Reading UK
Design considerations in the sequential analysis of matched case-control data

Tom Loeys
Department of Applied Mathematics and Informatics, University of Ghent, Krijgslaan 281, B-9000 Ghent, Belgium
A causal inference with survival data in a proportional hazards framework
Didier Renard
Centre for Statistics, Biostatistics, Limburgs Universitair Centrum, Universitaire Campus, Building D, B-3590 Diepenbeek, Belgium
Validation of a longitudinally measured surrogate marker for a time-to-event endpoint

Samuli Ripatti
Rolf Nevanlinna Institute, PO Box 4, FIN-00014, University of Helsinki, Finland
Joint modelling of genetic association and population stratification using latent class models
Sarah Zohar
Département de Biostatistique et Informatique Médicale, Hôpital Saint-Louis, 1 Avenue Claude Vellefaux, F-75475 Paris Cedex 10, France
Phase I and II dose-ranging clinical trials: Proposal of a two-stage Bayesian design

Book Review by Bruno Cesana (Italy)

Analysis of Pretest-Posttest Designs, by Peter L. Bonate, CRC (2000)

This book deals with a subject that has been considered in a very large number of papers and a very exhaustive "old" book "Problems in Measuring Change" (C.W. Harris Editor, University of Wisconsin Press, 1963), as can be seen from the long list of references: 127 unnumbered items listed in alphabetic order (pages 193 – 202) from the paper by F.M. Lord (Chapter 2 of Harris's book) to a number of more recent papers published in 1997.

The Author's statement in the Preface that "if I couldn't understand a paper after reading it once or twice or if it couldn't be easily implemented using readily accessible computer software, it wouldn't be included in the book" is rather surprising since many papers on this subject are not very easy to understand, particularly by a non-statistical readership Readers have to rely on the Author's understanding capabilities for having a definite explanation of the more "difficult" papers.

I tried to pick out everything that I found questionable (or more) from the statistical point of view, but can make no claim of being exhaustive because there are so many of these points. I shall, therefore, limit myself to describing the topics treated and making a few comments on each.

The book is divided into 10 chapters, and has a useful Summary section at the end in which the main questions are underlined.

Chapter 1 (Introduction) gives a general overview of the problems involved in Pretest-Posttest Designs. On page 8, the Author should write "As seen in Figure 1.3, when α is decreased, β, or the probability of not rejecting the null hypothesis given that it is *false* increases, and 1-β, or power, *decreases*".

The legend to Figure 1.3 also has to be corrected in this way, since the probability of not rejecting the null hypothesis, given that it is true, is equal to 1-α.

Perhaps, the whole text has to be read as: "The researcher may *increase* the probability of committing a Type I error (i.e.,α). As seen in Figure 1.3, when α is *increased* (from 0.01 to 0.05, for example), 1-β, or power, increases".

Page 10 gives Cohen's formula (1988) for the apparent effect size for paired data. I only have Cohen's first book of 1969, but it includes a short paragraph on page 13 showing that, instead of a simple study of sex differences concerning a defined ability, it may be better to plan comparing the means of males and their sisters and, "because of the removal of the variation between families, the effective standard deviation will be reduced to a fraction $\sqrt{(1-r)}$ (where r is the correlation coefficient between siblings)". I therefore disagree with Bonate when he says that this formula is appropriate for the case in which the "measurements are made on the same subject". Given the difference between the pre and posttest values, and assuming equal variances, the variability of the phenomenon is obviously equal to $\sigma\sqrt{[2(1-\rho)]}$, as the Author shows for the variance (equation 3.10 on page 53). Furthermore, on page 46 of Cohen's book (Case 4: One Sample of n Differences between Paired Observations), there is the correct effect size formula (2.3.5) of $d_z = m_z / \sigma_z$ where $\sigma_z = \sigma_{x-y} = \sigma\sqrt{[2(1-r)]}$, formula (2.3.7), in the case of $\sigma^2_x = \sigma^2_y$.

At this point the reader is practically sure that the analysis of the change (difference between pre and posttest) is more efficient than that using posttest scores. It could perhaps be useful to read Chapter 7 – Analysis of Covariance and the Study of Change in "The Design and Analysis of Clinical Experiments" by J.L. Fleiss (John Wiley & Sons, 1986) which Bonate does not mention in his bibliography. In this book, it has been clearly demonstrated that the simple analysis of change will not achieve the goal of obtaining less variability than when analysing only post-treatment values unless the correlation coefficient between the pretest and posttest values is more than 0.5. However, such a decrease can always be obtained by means of covariance analysis.

I do not completely agree with the Author's sentence on page 13 that "the pretest and posttest scores appear (from Figure 1.5) to be normally distributed". A few lines later, the statement "Obviously, for the expected increase in power with pretest-posttest data to be effective, the correlation between pretest and posttest must be greater than 0" should read "grater than 0.5" (or more generally in the case of unequal variances of the pre and posttest distributions, greater than the ratio between the pretest variance and twice the posttest variance).

Chapter 2 deals with several questions: What is Validity? What is Reliability? On page 23: E(C) = 0 (in the text) should read E(C)=C (C=0 if there is no systematic measurement error), Equation 2.6, instead of E(X)=T+C, should read: E(X)=E(T+C) = μ+C (since E(T)=μ). Furthermore, the second part of expression 2.6 "= $\mu + S_i + C$" should be μ+C since E(S_i)=0, as it is described in the text immediately below the equation that "the mean score is a function of the true score plus a component due to systematic error".

On page 25, the statement "if we subtract the population mean from both sides of equations (2.11): $X_{1i}=\mu+S_i+R_{1i}$ and (2.12): $X_{2i}=\mu+S_i+R_{2i}$ we obtain: 2.14: $(X_{1i}-\mu) = (S_i - \mu) + R_{1i}$ and 2.15: $(X_{2i} - \mu) = (S_i - \mu) + R_{2i}$" is not correct.

The derivation of the test-retest reliability or reliability coefficient between two measurements on page 25, is rather tortuous and involves a number of unjustified and unnecessary steps. It is difficult to believe that a reader can understand the plain idea that the reliability coefficient is the ratio between the variance of T (the subject's error-free score) and the variance of the observed score X (X = T + e), which is calculated only to obtain an index that is equal to 1 in the case of perfect reliability (when the error variance is equal to 0). In my opinion, the Author could improve his presentation by following the very clear explanation of reliability in J.L. Fleiss' "The Design and Analysis of Clinical Experiments" with all of the related aspects of the test-retest problem. The explanation and derivation of the reliability coefficient or the correlation coefficient between two measurements of the same subject could be made more understandable (even to a non-statistical readership) by giving a demonstration based on expected value algebra.

Chapter 2 continues with another relevant question: "What is Regression Towards the Mean?": Figure 2.2 on page 32 has been built using two different scales on the x and y axes; difference on the y-axis is less, but the mean of X is not well placed if the scales of the two axes are equal; it should be at about the same position as the mean of Y, since they are very similar. Otherwise, if the scale of the x-axis is the same as in Figure 2.1, the distance between Y' and the mean of Y is actually more than that from X' to the mean of X.

It is only in Table 2.2 that we discovered the data were simulated with a correlation coefficient of about 0.80, which explains why the plotted data in Figure 2.1 form an ellipse. On page 34, the same conditions (G<1 and x>μ) lead to a different conclusion.

"Why is Regression Towards the Mean Important?", "What is Pretest Sensitization?" are asked on page 45. There are some problems in derivation of 2.39, because equation 2.38 can be obtained only if the reader put $\mu_i = \mu + S_i$; furthermore, in equation 2.37, μ should be μ_i etc.

"Controlling for Pretest Sensitization with Factorial Designs" is the final topic of this chapter. On page 48, in the case of statistical significance of the interaction term, it is not clear what is different between the proposal of Jaccard (1997) of "testing the effects of the independent variable (the treatment) only at each level of the moderator" (previously defined as the pretest measurement, but in this case, the reader has to imagine that it is in some way discretized) and the standard approach of testing the simple effects.

Chapter 3 deals with Difference Scores, and is divided into various sections: Definition and Assumptions, Case 1: The Absence of a Treatment Intervention Between Measurement of the Pretest and Posttest Scores, Case 2: The Application of a Treatment Intervention Between Measurement of the Pretest and Posttest Scores, Nonparametric Alternatives to Case 1 or Case 2, Case 3: Two Groups with Different Treatment Intervention Between Measurement of the Pretest and Posttest Scores (A Controlled Study Design), Case 4: More Than Two Groups with Different Treatment Intervention Between Measurement of the Pretest and Posttest Scores (A Controlled Study Design), Unreliability of Difference Scores, Distribution of Difference Scores and Effect of Regression Towards the Mean on Difference Scores.

On page 53, equation 3.10 correctly shows the variance of the difference scores, from the previous assumptions as: $2Var(x)[1-\rho]$, but the conclusion "will have greater precision than the sum of the variances" is obvious, and the following text "For this reason, an increase in precision means difference scores are analyzed instead of posttest scores" is only true for $\rho>0.5$. On page 61, The use of the Latin instead of Greek letters for the statistic obtained would be more appropriate. For example it states "a natural estimator for τ_1 is $\bar{\Delta}_1$ whereas d_1 would be more better. Furthermore, $(\bar{\Delta}_2 - \bar{\Delta}_1)$ is the numerator of the t-test (see equation 3.30). There is also given $t_{\alpha(2),n-1}$ instead of $t_{\alpha/2,n-2}$ as the percentile of the Student's t distribution for rejecting the null hypothesis.

On page 63, an example is given using the posttest scores obtained from two groups (males and females). The example shows that the analysis of the posttest scores gives a statistically significant difference between the two groups, but the analysis of the differences between the pretest and the posttest scores gives a non statistically significant difference: this is obviously due to the considerable difference between the mean baseline scores of the two groups (obtained without using a randomization procedure). The following sentence: "Ignoring the influence of baseline differences on psychomotor impairment would have lead (perhaps led) to a Type I statistical error, i.e., rejecting the null hypothesis when false" is beyond comment!.

Page 63 also has another example of a not sharable statistical reasoning: the Author uses Shapiro-Wilk test to test the null hypothesis that the baseline score and the posttest score are normally distributed; having not rejected the null hypothesis, he also performs the test on their difference, in this case obtaining a statistically significant result leading to the rejection of the null hypothesis that the difference between the pretest score (accepted as being normally distributed) and the posttest score (again accepted as being normally distributed) is not normally distributed! This conclusion goes against the well-known elementary statistical notion that the difference between two normally distributed variables is normally distributed, as the Author states at the bottom of page 68.

If the normal assumption has to be tested, it can be done using only one test carried out on the variable that will be used in the statistical test of the null hypothesis also in order to avoid increasing the probability of making a Type I error. Furthermore, using Bonferroni's correction of the significance level for three tests gives a probability value of about 0.017, thus allowing a p value of 0.0349 to be considered not statistically significant.

Chapter 4, Relative Change Functions, considers Definitions and Assumptions, Change Scores and Regression Towards the Mean, Difference Scores or Relative Change Scores, Other Relative Change Functions, and Distribution of Relative Change Scores. On page 84: "although modified change scores ((Y-X)/[(Y+X)/2] from equation 4.15 at page 82) improve the sampling distribution properties by making them more symmetrical compared to percent change scores, there are still many cases where they are not normally distributed". From the theoretical point of view they cannot be normally distributed. After equation 4.17 dealing with the log percent scores, the same sentence is repeated, but it is not clear if the sentence here refers to the log percent scores or not. In any case, this sentence has to be considered as not correct.

On page 85, the Author shows the results of a simulation study "conducted to test the hypothesis that if the pretest and posttest are normally distributed, then the distribution of the relative change scores will also be normally distributed". At this point the results obtained using the omnibus test proposed by D'Agostino et al. (1990) are used to conclude about the normal or non-normal distribution of the "percent change scores", the log-ratio scores and the modified percent change score obtained from normally distributed pretest and posttest scores. However, starting from the well-known statistical notion that all of these relative changes are not normally distributed, I think that these results can only be used in the context of a power study.

The point that distributional properties have to be considered from the mathematical and statistical point of view, and not from the results of a statistical test subject to Type I and Type II error probabilities, is completely missed throughout practically the entire book.

Chapter 5 deals with Analysis of Covariance (ANCOVA). After having described the Definitions and Assumptions, the Author prefers to address the interested reader to other books and to consider the basic assumptions of the ANCOVA and the special issues in using ANCOVA in the analysis of pretest-posttest designs.

Parametric ANCOVA, ANCOVA with Difference Scores as the Dependent Variable, ANCOVA using Percent Change as the Dependent Variable, The Assumptions of the ANCOVA are considered in detail. Violation of Homogeneity of Within-Groups Regression Coefficients and the nonparametric approaches proposed if this assumption is not fulfilled are also highlighted. Quade's (1967) procedure is illustrated and useful results comparing the robustness of parametric and nonparametric ANCOVA are also considered in detail.

Error-in-variables ANCOVA: in this part it would be more useful to consider briefly the case in which the covariate is a random variable rather than a mathematical variable (as in classical regression analysis) before extending the case to a random variable with measurement error. In the section Assumptions of the ANCOVA, the statement that "the pretest scores are measured without error" is perhaps not clear enough to convey the fact that the covariate can be a mathematical or a random variable without the problems involved in the "error-in-variables" model.

Further points of Chapter 5 are Other Violations (curvilinear relationship), Effects of Outliers and Influential Observations. On page 103, the term e_{ij} in equation 5.19 of the predicted value should not be added; this paragraph considers the importance of the presence of outliers and the iteratively reweighted least squares is described together with the performance of the Huber function or bisquare function.

Chapter 6 deals with Blocking Techniques, and considers stratification, blocking or post-hoc blocking techniques. In this section "Using Stratification to Control for the Pretest" the phrase on page 113 "power was greater than 0.6" should read "correlation coefficient was greater than 0.6". "Post-hoc Stratification" is also considered, and the Author's point of view that its use should be discouraged is completely sharable.

Chapter 7 deals with "Repeated Measures Analysis of Variance". In the section Using Repeated Measures ANOVA for Analysis of Pretest-Posttest Data, equation 7.1 on page 117 would be clearer if the terms and their indices were given together rather than showing the terms after their indices.

The Author then underlines the difference between the repeated measures and the pretest-posttest designs according to Huck and McLean (1975). If subjects are measured prior to randomization to a treatment group, and then an additional measurement is collected after the treatment intervention, the model is different from the one outlined in equation 7.1 (which assumes that all measurements are made after the treatment intervention); in this case, equation 7.3 (in which a β_1 term is missing in my opinion and also according to equation (2) of Huck and McLean, 1975) and equation 7.4 are pertinent. The Huck & McLean paper was written in 1975 in order to stress the fact that a differential treatment effect has to be assessed using the interaction "treatment by time" term. Although this is now very well known, it is still worth considering in depth.

On page 120, equations 7.5 and 7.6 are based on a notation that has not previously been explained, and there is the statement " …Thereby increasing the probability of committing a Type II error (failure to reject the null hypothesis when it is true)"; rather than believe that this a very personal point of view of the Author, I assume it is another typographical error ("true" instead of "false").

There are also some misunderstandings. Like all statistical tests, the F test does not provide an estimate of the "true treatment effect". Statistical tests test a null hypothesis and do not estimate effects. In their paper,

Instead of being shown by a data example, the fact that the "F test of the interaction effect (treatment by time) and the F-test from an analysis of difference scores will always be the same" would be more soundly shown using the definition of the interaction in the case of a pretest-posttest design. On page 121, the Author wrote "…but also assume a particular variance/covariance structure between the observation which must be specified in the linear model" without any further explanation that this assumption is neither necessary nor sufficient in the case of a pretest-posttest design in which only two measurements are made of the same subject.

The other topics in Chapter 7 are: Regression Towards the Mean with Multiple Posttest Measurements, Using Repeated Measures ANOVA for Analysis of Pretest-Posttest Data with Multiple Posttest Measurements (referring to other Authors), and Analysis of Repeated Measures Using Summary Measures. On page 128, he says that "traditional repeated measures analysis using time as a categorical or continuous variable is useful because it allows for isolation of specific time periods where differences may occur between treatments". This issue is very frequently raised by clinicians who ask "When is there a statistically significance difference between the investigated treatments?", being completely unaware of the fact that, if a statistical difference is demonstrated (say) in the second week, this does not mean that the treatments are "truly different" only from then and not beforeIt is much more interesting (and sounder) to consider the temporal trend (linear, quadratic etc.) of the possible differential effect of the treatments under investigation. This is a question that needs to be addressed to the non-statistician counterparts of scientific research.

Chapter 8 deals with Choosing a Statistical Test and shows the validity of some statistical tests by means of a Monte Carlo simulation study. Choosing a Test Based on How the Data will be Presented is an unfortunate title; perhaps "based on the design model" would have been better. On page 136, the sentence "Each of the tests may have different Type I error rates" is quite difficult to understand: under the null hypothesis, and if all of the assumptions underlying the statistical test are fulfilled, the Type I error of a statistical test is just the chosen threshold of statistical significance. The other sections include: Monte Carlo Simulation When the Assumptions of the Statistical Test are Met (on page 128, the covariate for the ANCOVA analyses is wrongly written as the posttest instead of the pretest scores), Monte Carlo Simulation When Systematic Bias Affects the Pretest and Posttest Equally, Monte Carlo Simulation When the Variance of the Posttest Scores Does Not Equal the Variance of the Pretest Scores, Monte Carlo Simulation When Subjects are Grouped *A Priori* Based on Pretest Scores (Randomized Block Designs), Monte Carlo Simulation When the Marginal Distribution of the Pretest and Posttest Scores was Non-Normal.

The results shown in this Chapter 8 are not only difficult to understand for a non-technical reader without a more exhaustive explanation of the reasons for which this procedure can be used, but are also quite surprising. On page 141, it is said that "when the correlation between pretest and posttest was marginal to large, ANOVA on posttest scores alone cannot be recommended as the drop in power decreases rather steeply as the correlation between pretest and posttest increases". I think that this statement should be commented on or justified in more detail.

I performed the same simulation study in an attempt to understand what seemed to me to be very strange results. First of all, before undertaking a simulation study of the power of some statistical tests, it is useful to calculate the "expected power" in order to be able to compare the relative frequency of the statistically significant results obtained against a "reference value". In the given example with $\sigma^2 = 1.0$ for all distributions, the power $(1-\beta)$ is 0.45799 and 0.97326 for the case $\mu_c = 0.0$ / $\mu_1 = 0.5$ / $\mu_2 = 1.0$ and $\mu_c = 0.0$ / $\mu_1 = 1.0$ / $\mu_2 = 2.0$, respectively. In the first case, I obtained 44.9% and 46.8% statistically significant results with $\rho = 0.0$ and 0.8; in the second case I obtained 97.2%, 97.0% and 96.9% with $\rho = 0.0$, 0.8 and 0.95. Therefore, if the pretest and posttest scores are in the same way correlated in the three groups, the effect of the treatment on the posttest score has to remain unchanged; of course, in the case of a correlation greater than 0.5, the variability of the difference scores analysis will decrease in comparison with that of the posttest scores. I think that the Author obtained his results by fixing the maximum effect size at 2 and using equation 1.5 (as he said explicitly on page 137) and, so for $\rho = 0.95$, the numerator becomes 0.4472136 leading to $\mu_c = 0.0$ / $\mu_1 = 0.2236068$ / $\mu_2 = 0.4472136$. In this case, the expected power is 0.12351 and I obtained 11.8% of statistically significant results. In conclusion, the effect size for this kind of study has to consider the difference (between the more efficacious treatment and the control) standardized by the variability of the investigated phenomenon which, in the case of the difference between pretest and posttest scores with equal variances, is $\sigma\sqrt{[2(1-\rho)]}$. Furthermore, the intermediate treatment effect can be put at the mean value between the control and the maximum treatment effect. At this point, I think that all of the conclusions of this simulation study have to be dropped.

Chapter 9 deals with Randomization Tests and Permutation Tests and Randomization Tests. On page 162, it is said "When the test statistic requires a certain underlying distribution to obtain a valid p-value then we say that that test is a parametric statistical test". It would be better to make a distinction (if only for the sake of being accurate particularly in a "teaching context") between nonparametric procedures that are not concerned with population parameters and those that are distribution-free. Furthermore, a sentence about the difference between Randomization Tests (the basis for permuting the data is random assignment) and Permutation Tests would also be useful for the sake of accuracy.

Other topics considered in some detail are: Analysis of Variance (on page 165, "The residuals from the ANOVA were not normally distributed (p=0.0006)" instead of the "null hypothesis of a normal distribution was rejected"), Analysis of Covariance, Resampling within Blocks or Time Periods and Resampling with Missing Data. SAS programs are given in the Appendix but I did not check them (perhaps a floppy with the written programs could be supplied with the).

Chapter 10 deals with Equality of Variance and Methods and Procedures. The statistical test for testing the null hypothesis of equality of two variances is shown starting with the approach of testing the null hypothesis of homoscedasticity of dependent random variables using the correlation coefficient between the difference and the sum of two random variables proposed by Pittman (1939) and Morgan (1939). It must be pointed out that the difference Y-X in Equation 10.3 has to be reversed in order to obtain the difference between the variances of X and Y, but the essence of the test does not change at all; furthermore, a more formal demonstration, such as: Cov(Y-X,Y+X) = E[(Y-X-E(Y-X)][Y+X-E(X+Y)] would be more demonstrative from a teaching point of view.

On page 176, the conclusion is not easy to understand. The Author says that the Pittman-Morgan test has to be preferred, but then adds, as the third point, that "in this example the marginal distribution of the posttest was not normally distributed (once again instead of "the null hypothesis was rejected"), suggesting that some nonparametric alternative to the traditional Pittman-Morgan test be used. For these reasons, it should be concluded that the variances were equal. A few lines later he says "Wilcox (1989, Psychometrika, 54,305) provided a statistic to test whether the variance of q groups with pretest posttest data have equal variance".

Concluding remarks.

This book deals with all of the most important issues of pretest-posttest design. Some points could perhaps be explored in more detail (such as the Covariance analysis, for example), but this is really just a matter of reader, reviewer and Author preferences. However, it must to point out that some points are considered in much more details because of the Author's personal taste rather than their actual relevance to this kind of design.

However, the book is unfortunately full of sentences and conclusions that are not acceptable from the statistical theory allowing it not to be recommended, particularly for a scholarship. This is a real pity since the general coverage is good and the review of the statistical papers made in some chapters is quite exhaustive.

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ISCB22 AGM of ISCB 2001 in Stockholm

From Emmanuel Lesaffre

The Annual General Meeting (AGM) will be held in the main conference hall following the President's Invited Keynote Lecture on Tuesday 21, between 12 and 1 PM. The agenda is the following:

1. President's report
2. Treasurer's report
3. Subcommittee reports: Fraud, Statistics in Regulatory Affairs, Education, National Groups, Communications, Student Conference Awards, Operating Procedures
4. Nominations: there is one vacancy for the Executive Committee.
5. Future ISCB meetings: 2002 Dijon (F), 2003 London (UK), 2004 Leiden (NL), 2005: ?
6. Any other business

All participants of the Stockholm meeting are by definition ISCB members are, therefore, most welcome to attend. Please plan to take part !

Call for Nominations for Position on the ExCom

From Emmanuel Lesaffre

ISCB will need nominees to fill 1 ExCom positions for 2002-2003. For further information, please contact the Secretary.

Information on Submitting Articles

Articles sent via e-mail 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.

Advertising Rates

The prices are:			**Additionally, we will include loose flyers with the distribution of the newsletter at an initial handling cost of £ 150. 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 Editor.**
Full	**A4 page:**	**£ 200**	
Half	**A4 page:**	**£ 150**	
Quarter	**A4 page:**	**£ 100**	
Publishing dates		**2001**	**(early October)** **December**
(and deadlines)		**2002**	**(early May, October)** **June, December**

IMPORTANT NOTE: E-mail 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 announcements can be sent as an e-mail to members by the ISCB egroup (currently free of charge, but under review and subject to the Editor's and Officers' decision).

ISCB 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

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ISCB: Changes of Address or E-mail

Please inform the Permanent Office that looks after the membership and mailing list databases. Also, if your **e-mail address changes**, please inform the Office and the News Editor so that your address is changed in the ISCB database and egroup.

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.

Previous meetings in recent years have been held in Boston (1997), Dundee (1998), Heidelberg (1999) and Trento (2000). 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 Analysis of Ordered Categorical Data, Cross-over Trials in Clinical Research, Analysis of Repeated Measures, Survival Analysis, Extending the Cox Model, and Statistical Methods for Genetic Epidemiology.

The current composition of the **Executive Committee** (ExCom) for 2000 is as follows:

Officers:
President: Mr Simon Day (UK),
Vice-President: Prof. Maria Grazia Valsecchi (I),
Secretary: Prof. Emmanuel Lesaffre (B),
Treasurer: Prof. John Whitehead (UK), and
Members:
Newsletter Ed.: Dr David Warne (CH),
Webmaster: Mr Bjarne Nielsen (DK),
Past-President: Dr Nancy Geller (USA), and
Dr Elia Biganzoli (I), Dr Harbajan Chadha-Boreham (CH), Prof. Stephen Evans (UK), Dr Siem Heisterkamp (NL), Prof. Carol Redmond (USA), Dr Julia Singer (H), Prof. Elisabeth Svensson (S) and Prof. Norbert Victor (D).

The annual general meeting of the ISCB is organised to coincide with the scientific meeting. Membership of the Society is drawn from more than 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** 2 or 3 times a year. The ISCB News editor is Dr David Warne, Chemin Frank-Thomas 40, CH-1208 Geneva, Switzerland. Items for inclusion in the Newsletter should be sent to him (if possible on a 3.5' disk, Word, RTF, HTML or text, or e-mail) to:
100557.2260@compuserve.com

Membership of the Society is open to all with an interest in biostatistics. The current annual (to 31 December 2001) Ordinary membership fee is £15. The Full-time Student Membership fee is £7.50. Members can also choose to receive Statistics in Medicine at a reduced cost (see above), and benefit from the reduced conference fee, at least £15 less than for non-members.

Applications for membership should be sent to:
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Tel: +45 48 484 100,
Fax: +45 48 484 200,
e-mail: Iscb@post3.tele.dk
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Calendar

23-28 July 2001 — **Hamburg, GERMANY**

Mixtures 2001: Recent developments in mixture modelling

Info: Wilfried Seidel, FB Wirtschafts- und Organisationswissenschaften, Universität der Bundeswehr Hamburg,
D-22039 Hamburg, GERMANY.

e-mail: mixtures@unibw-hamburg.de , web: bruce.unibw-hamburg.de/mix01

19-23 August 2001 — **Stockholm, SWEDEN**

ISCB22

Info: Clinical Data Care, Warfvinges Väg 16, S-11251 Stockholm, SWEDEN

Tel: +46 8 618 2280, Fax: +46 8 618 2281,
e-mail: theresa.westerstrom@ISCB.stockholm2001.org , web: www.ISCB.stockholm2001.org

21-26 July 2002 — **Freiburg, GERMANY**

International Biometric Conference 2002

Info: Kongress & Kommunikation gGmbH, Hugstetter Str. 55, D-79106 Freiburg, GERMANY

e-mail: kkkri@ukl.uni-freiburg.de, web: www.ibc2002.uni-greiburg.de

9-13 September 2002 — **Dijon, FRANCE**

ISCB23

Info: Harbajan Chadha-Boreham

e-mail: h.chadha-boreham@fournier.fr

20-24 July 2003 — **London, ENGLAND**

ISCB24 joint with Society for Clinical Trials

Info: Diana Elbourne

e-mail: diana.elbourne@lshtm.ac.uk