



# International Society for Clinical Biostatistics

Number 8

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Editor: Mats Lörstad

## ***FROM THE PULPET OF THE PRESIDENT:***

Dear Colleagues,

Writing down these lines for the ISCB-newsletter my memories are going back to our last meeting in Maastricht. On my way to the conference I travelled to Aachen and changed to the train which passed the German-Dutch border and went to Maastricht. On this train I met two colleagues from the German Democratic Republic (GDR). They were astonished that the border to the Netherlands was invisible and not detectable. Additionally they were surprised that we arrived in Maastricht not only without any customs and passport control but also without having seen any German or Dutch police. We all agreed that this way of travelling from one country to another was ideal but not realistic for the near future in Eastern Europe.

During the ISCB meeting in Maastricht, Hungary began to open the border to Austria. Now only seven months later we all have seen the pictures, which showed the dramatic changes in Eastern Europe: the opening of the Berlin wall, the democratic elections in Poland, Hungary and GDR, the peaceful revolution in Czechoslovakia and the violent end of the Ceausescu regime in Romania. Thus my personal hope of a Europe without borders is perhaps not a fantasy but a realistic possibility in the not too distant future.

Since the ISCB meeting in Innsbruck, where I was elected Vice-President, I tried to increase the number of ISCB members from Eastern European countries. The most difficult problem was the non-convertible currency in these countries. In order to solve this problem we created the following model for such a country:

One colleague is acting as the National Representative of the ISCB in that country. He gives information about the ISCB to interested scientists in that country and tries to recruit them for the ISCB. He opens an ISCB-account, where all ISCB-members from that country can pay the membership fee in their own currency. For participants of ISCB-meetings it is also possible to pay for registration and housing into that account. The costs for registration and housing for the National Representative is paid by the ISCB. Additionally, if a national section of ISCB is built up, one free subscription of "Statistics in Medicine" for this section goes to the National Representative. The final aim is to organize in some future years an ISCB-meeting in that country.

In the meantime this model was introduced in Poland and the GDR. The USSR and Hungary could follow this year. I hope I can contact colleagues in Czechoslovakia and Romania during the next months.

The next ISCB conferences after Nîmes, France will be 1991 in Brussels, Belgium and 1992 we have plans for Copenhagen, Denmark. Basle, Switzerland is a candidate for 1994. I hope that the positive developments in Eastern Europe will continue and that ISCB conferences will take place in Warsaw, Prague, Moscow, Leipzig or Budapest.

My best wishes for all of you and "Au revoir" in Nîmes.

Wolfgang Köpcke

## **JØRGEN SELDRUP - ISCB HONORARY SECRETARY 1987-90**

When the Nîmes meeting comes around in September, Jorgen will have completed four arduous years as Secretary of the ISCB. In accordance with the constitution he will then have to stand down. (The full implications of his move will be apparent to all of us, the more apprehensive of the ISCB future we are, the more we will miss Jorgen). Since this moment should not go by without proper recognition, the ISCB-News has made this attempt to get a close-up on Jorgen using his own responses to piercing questions aimed at telling his fan club the real truth.

Q: So, Dr Seldrup, is it your cultural inheritance or your experience from various environments that has enabled you to keep this Society together for the latter part of the eighties?

A: I was born in Denmark, some 48 years ago, on some days it feels rather more, on others less. I studied mathematics and later statistics at Aarhus University (and in Danish, ed.) With this knowledge I felt the urge to follow in the footsteps of the ancient vikings and go teach the English a lesson or two. Thus I started with the Geigy Pharmaceuticals which later was turned into Ciba-Geigy Pharmaceuticals. Since I was their first statistician ever (in 1970), I am pleased to report that my first reports are hard to find and can be described as nothing less than collectors' items. But my dogged determination to dig deeply into the data did make its mark.

Q: And you became a permanent fixture at Ciba-Geigy...?

A: As a matter of fact, even though the department grew and people came and left, I could never make up my mind to leave so I stayed on and on and on, until last year when my decision process had ripened. And when I move, I move over fire and water! I decided to try my third country and language to become Director of Biostatistics at ITEM, Institut Technique pour l'Etude du Médicament, a clinical research contract organisation, based in Paris. In France, to be exact (I understand the French have an obsession with exactitude so I am trying my best).

Q: You have been very creative in inventing reasons to leave home to meet with other statisticians. Tell the readers about your accomplishments. And what does your wife think?

A: I founded and was the first chairman of PSI, Statisticians in the Pharmaceutical Industry. This was initially a small UK organisation but now a major European one with several hundred members. I also served on Council of the Biometric Society (British Region) and the Institute of Statisticians and have in that time been technical convenor of several statistics conferences on medicine, health and biometry. My wife is Danish.

Q: How come you turned your interests towards the ISCB?

A: At the ISCB San Marino meeting in 1985, I was trapped in a corner of the bar by Doug Wilson, who twisted my arm until I agreed to start the ISCB Newsletter. (And we are not even in the same weight category!). I edited its first three issues and as editors learn the hard way, editing means writing. My wit was exposed in my "Letters home" which may have gone unnoticed by the general public but nevertheless are considered as gems in contemporary biostatistical literature. But the major break came when I had the opportunity to channel my enthusiasm into the job as Secretary of ISCB in 1987, the same year as ISCB had its conference at the real outskirts of Europe, in Gothenburg.

Q: And when you are not statistizing, would you consider yourself a family man?

A: Well, I don't quite know where to place myself on such a scale. But my one and only wife Ulla and I recently celebrated 25 years of not always seeing much of each other. Our two sons, Erik and Ian, have chosen broader pathways than statistics. Erik is studying electronic engineering at York University and Ian is about to start his course in astro-physics at Sheffield University. From their bases they promise to come and look after their old folks in Paris. I hope many of you will do the same.

# ***NOW TO NÎMES AND ISCB-11***

## **SCIENTIFIC PROGRAMME**

The main objective of ISCB meetings is to create an opportunity for the exchange of knowledge, ideas and methods between clinicians, epidemiologists, statisticians and members of other disciplines (pharmacologists and biologists).

The Nîmes Conference will focus on selected themes such as Statistical Aspects of AIDS, Methodology of Phase I and II trials, Epidemiologic Methods, Repeated Measurements and Multivariate Analysis. Clinical Trials remain a theme of interest with an opening lecture, four contributed sessions and an ISCB course on Sequential Methods in Clinical Research.

### ***INVITED SPEAKERS***

#### **Tuesday, September 18, 1990 Inaugural Session**

David P. BYAR (USA) Clinical Trials: Adapting to New Challenges

Jacques BENICHO (France) Attributable Risk: Adjusted Estimation Methods from Case-control Studies

Walter LEHMACHER (FRG) Multiple Testing with Two Groups of repeated Measurements

#### **Wednesday, September 19, 1990 AIDS Session**

Klaus DIETZ (FRG) Parameter Estimation for AIDS Models: a Survey

Valérie S. ISCHAM (UK) Modelling and Prediction of the AIDS Epidemic

Ronald BROOKMEYER, J. LIAO (USA) Statistical Modelling of the AIDS Epidemic for Forecasting Health Care Needs

Dominique COSTAGLIOLA, Nathalie RUDE, Marguerite GUIQUET, Alain-Jacques VALLERON (France) Models for the HIV Infection in France: Risk Groups and Clinical Stages

Mitchell H. GAIL, P. S. ROSENBERG, J. J. GOEDERT (USA) Therapy May Explain Resent Deficits in AIDS Incidence

#### **Thursday, September 20, 1990 Phase I and II Session**

Jean-Louis STEIMER (Switzerland) Non Linear Regression Modelling In Pharmacokinetics during Preclinical and Clinical Drug Development

John O'QUIGLEY, Sylvie CHEVRET (France) Sequential Design and Analysis of Dose Finding Studies in Patients with Life Threatening Disease

John WHITEHEAD (UK) Statistical Aspects of Phase II Clinical Trials

#### **Friday, September 21, 1990**

**Advances in Medical Statistics over the last Decade** (Session devoted to Statistics in Medicine)

Douglas ALTMAN (UK) Statistics in Medical Journals

Martin SCHUMACHER, M. OLSCHESKI, G. SCHULGER (FRG) Assessment of Quality of Life in Clinical Trials

P. K. ANDERSEN (Denmark) Survival Analysis: The Second Decade of the Cox Model

#### **Closing Conference**

Yves ESCOUFIER (France) L'Analyse des Données in Practice

### ***CONTRIBUTED SESSIONS***

Contributed papers are planned for the afternoons either in parallel sessions or in one poster session. The preliminary schedule focuses on the announced session themes of the ISCB 11 conference: Randomized Clinical Trials, Epidemiologic Methods, Multivariate Analysis, Repeated Measurements, Statistical Aspects of AIDS, Methodology of Phase I and II Trials.

**ISCB-11 Course:  
SEQUENTIAL METHODS IN  
CLINICAL RESEARCH**

**MONDAY SEPTEMBER 17, 9 am – 5.30 pm**

**Introduction**

There is a growing interest in the use of sequential methodology for clinical trials. Within this course, the term "Sequential Methodology" is interpreted widely and includes group sequential methods and interim analyses. The design of sequential studies and the derivation and properties of various forms of stopping rule are covered. Emphasis is given to valid methods of estimation at the end of a sequential study. Case studies are used for illustrations. Practical exercises are set to aid comprehension. The micro-computer package PEST (Planning and Evaluation of Sequential Tests) is used as a teaching aid.

**Audience**

This course is intended for people engaged in clinical research. An understanding of conventional methods for designing and analysing clinical trials will be assumed. The emphasis is on the use and the interpretation of sequential trials. Mathematical details are avoided in order to make the course accessible to those without formal training in mathematical statistics.

**Presenters**

John Whitehead, Hazel Brunier, Karen Facey from Department of Applied Statistics, University of Reading, England.

**SOCIAL PROGRAMME**

**Monday September 17, 1990**

Welcome party at 7 pm, Cesar Palace (location of congress)

**Tuesday September 18, 1990**

- Walking guided visit of the old Nîmes (6 to 8 pm)
- Reception hosted by the Mayor of Nîmes in the Mairie de Nîmes (8 pm)

**Wednesday September 19, 1990**

Conference Dinner in a traditional farm in Camargue (Departure: 5.15 pm)

**Thursday September 20, 1990**

Visit to the Pont du Gard (6 to 8 pm)  
Reception hosted by the President of the Conseil du Gard in the Hotel du Département

**Friday September 21, 1990**

Beginning of the Feria des Vendanges, a three-day bull fight.

**QUALITY OF LIFE: NÎMES**

Nîmes is the prefecture of the department of Gard, in the South of France, between Provence and Languedoc. Nîmes has got magnificent monuments from the Roman period and is called "The French Rome" ("La Rome Française"). Among the most striking monuments are the roman amphitheatre in which performances are still held today, the Maison Carrée, a gallo-roman temple dedicated to Augustus' grandsons, and ramparts built by Augustus.

Nîmes is only a short drive away from the Camargue region, realm of bulls and horses, in which one can enjoy horseback riding, safaris in four-wheel drive vehicles or boat trips to the sea. In the South of the Camargue region, the medieval City of Aigues-Mortes offer its renowned ramparts erected by the son of Saint-Louis in preparation of the approaching departure for the Crusades.

Another nearby site is the "Pont du Gard". This aquaduct-bridge is part of a 50 kilometer long aquaduct that transported water from Uzès to Nîmes. It is the highest bridge created by the Romans.

Other striking sites such as the medieval cities of Sommières and Uzès, the Cévennes region and grottos such as Trabuc and La Cocalière also deserve a special mention.

Among the culinary specialities of Nîmes are the "brandade de morue" made of dried filets of salted cod in the best olive oil and the "tapenade d'olives", a paste of black or green olives mixed with anchovies and aromatised with herbs of Provence.

In September, the weather is most pleasant in Nîmes. The ISCB conference will end at the beginning of a three day bull fight, the Feria des Vendanges.

## **ISCB-11 REGISTRATION FEES** (in French Francs)

	Before July 15, 1990	After July 15, 1990
Full Congress Fee	2 000	2 400
Speaker	1 700	-
Student	1 500	2 000
One Day Fee	800	1 000
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Sequential Methods Course	750	850
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Accompanying Person	1 000	1 200

Participant fees include admission to the congress, abstracts book, lunches, coffee breaks and social programme (except bull fight). For accompanying persons, fees include lunches and social programme.

### **Cancellation**

For cancellations received before July 31, 1990, a 20 % handling charge will be made.

## **ISCB MEMBERSHIP**

If you have not yet joined the ISCB, just because you are not fully informed on rates and procedures, the following information is intended to deprive you of that excuse!

### **RATES**

£ 15.00	Ordinary Membership of ISCB (to end 1990)
£ 7.50	Full-time Student Membership of ISCB (to end 1990)
£ 95.00	Ordinary Membership of ISCB (to end 1990) + UK Subscription to 'Statistics in Medicine', 1990 (NOTE: UK only)
£ 105.00	Ordinary Membership of ISCB (to end 1990) + Overseas, i.e. non-UK, only)

The information we require from you is the following:

Name, Title, Occupation (whether statistician, medical doctor, both or neither), Post held, Business address with post code and country. And if you are adventurous enough to send us money the treasurer very much appreciates to know the Cheque/Money Order No and the date it was sent. The following cheques, made payable to "The International Society for Clinical Biostatistics" are acceptable: a British Bank cheque, a Sterling Eurocheque or any cheque drawn in Sterling and payable in London on a named London bank.

Address: Dr Douglas Wilson, Hon. Treasurer ISCB, TENOVUS Institute for Cancer Research, Heath Park, CARDIFF, CF4 4XX, U.K.

Those wishing to communicate to the ISCB on general matters should write to: Honorary Secretary Dr Jørgen Seldrup, I.T.E.M., 93, Av. de Fontainebleau, F-94270 Le Kremlin-Bicetre Cedex, France.

## NEWS AND VIEWS FROM THE TREASURER

### Membership status

In recent years, membership of Society has remained reasonably stable. In the time span 1987-89, total annual membership to the Society was 251, 259 and 261 respectively. A breakdown of membership on a national basis for 1989 shows strong British support followed by France, Sweden, the federal Republic of Germany and the United States.

<u>1989</u>	
<u>Country</u>	<u>No of ISCB Members</u>
Australia	6
Austria	4
Belgium	13
Canada	6
Denmark	4
F R Germany	22
Finland	2
France	30
German D R	8
Great Britain	50
Hungary	1
Ireland	1
Israel	1
Italy	16
Japan	2
Kuwait	1
Netherlands	14
Norway	13
Portugal	1
Spain	10
Sultanate of Oman	1
Sweden	23
Switzerland	14
United States of America	18
<b>TOTAL</b>	<b><u>261</u></b>

Over the years the ISCB has gained many new members, largely as a result of the publicity for our conferences and largely through the hard work of the local organizing committees, but also we have lost members because their interest has not been sustained. It is my personal view that the ISCB membership could have been at least two or three fold more than it is today, particularly when the activities of ISCB are held in high regard. Some relevant points follow.

### The importance of the Membership to the ISCB

Members, of course, constitute the Society and from a Treasurer's viewpoint the

membership subscription fees form a vital component of our income which is just sufficient, with the interest received from our assets, to pay our expenses.

### The advantages of Membership

The Society now provides a Newsletter to Members twice a year, offers reduced subscription rates to "Statistics in Medicine" and it has been customary to offer our members reduced registration rates at our conferences. It is necessary that present and potential members of the Society are properly informed as to what these advantages are, and for the Executive Committee to ensure that these benefits are sustained.

### Problems with Membership

The ISCB does not have a permanent base for its secretarial and administrative activities; it depends of the work of the individual and, with every election of new Officers, moves from one centre to another and communication problems can arise. Considerable problems arose as a result of a postal strike in the United Kingdom resulting in cheques being out-of-date, problems in banking, and some difficulties were experienced with delivery of "Statistics in Medicine", all this preceding the change-over to a new Treasurer.

### The Organization of Finance Affairs and Members Subscriptions

A database management system has been in operation for sometime now and is completely up-to-date in so far as information is made available to the Treasurer. In 1990, the members have made an effort to help the Treasurer by complying with certain requests such as:

- (1) Ensure, if possible, payment and form are sent together.
- (2) If payment is sent by your company, please give them your details to accompany payment.
- (3) Please pay in the manner suggested. A cheque in US dollars, equivalent to £15 will be realized under £2.

A list of members will be provided for inspection at the Nimes meeting. Currently, the database system is being extended to help process subscriptions to "Statistics in Medicine".

### Planned improvements to the Service

It has been arranged with John Wiley that prices for "Statistics in Medicine" for 1991 will

be known before the ISCB-11 event. Therefore, subject to permission from the Nîmes Local Organizing Committee, it is proposed to collect subscriptions for 1991 in September. For those who will not be in Nîmes, a "call for subscriptions" for 1991 will be made early, namely late October so as to effect continuity in the delivery of "Statistics in Medicine". Already, credit facilities have been arranged with John Wiley, thus obviating the need, and time involved, in getting cheques countersigned before orders are processed. Finally, the possibility of payment of subscriptions using a VISA card will be explored as this would facilitate payment and, I am sure, bring in more members to the Society.

### Problems

Will the following people to which address is missing please correspond with the Treasurer – Cano, Hoclet, Boichut and Segu – as queries exist concerning their membership. Correspondence should be addressed to the Honorary Treasurer ISCB (address is given earlier). Telephone: 44 (222) 755944 Ext 2612, Fax: 44 (222) 747618

### Unpaid Subscriptions for 1990

It is possible that some "members" are awaiting the registration fee for the Nîmes meeting before paying their subscriptions. In any event for those who have not yet paid their subscriptions, please complete the enclosed form and send it to the Treasurer as soon as possible.

D W Wilson

### Ethics, a two-way street?

From Professor David Finney we have received the following story, which ought to bring forth some reaction from statisticians working in the pharmaceutical industry.

*"I was invited to attend a meeting, during which a young statistician presented some data for discussion. She gave signs of general competence, but obviously she had little experience and she was evidently at a loss how to handle what seemed to her an awkward point.*

*The data she presented included figures said to relate to a small group of subjects under observation for a week, and to be the percentages of days during which each subject was free from symptoms of the illness that was being studied. I noticed values such as 28.6, 14.3, 100, 57.1 and the like, all consistent with being  $k/7$  expressed as a percentage. My eye*

*was struck by an instance of 16.7, which could not occur with any integer value of  $k$ . I saw other similar anomalies in data from other batches of subjects from the same clinical trial. Naturally, I asked a question; I expected to be told that occasionally observations did not continue for a full week, and that 16.7% represented  $1/6$ ; I should then have wanted to inquire into possibilities of bias if, to suit someone's convenience, the length of observation period could be altered.*

*A more senior colleague of the speaker, who happened to be present, politely and tactfully asked me not to press my question, as this could embarrass the speaker. He explained that if, when she had received the percentages for analysis, she had gone to the senior clinician who had provided her with the data and asked questions about how the records were obtained, she would possibly have been regarded as making impertinent inquiries inappropriate to someone her junior status and she might even have received a formal reprimand!*

*I was astounded, but the matter was not of such immediate importance that I was prepared to intervene. Apparently, someone as junior as she was, could receive such percentages from a clinical investigator with a request for an analysis that involved comparing them with other similar data from subjects receiving a drug, and she would be expected to conduct this analysis without raising any questions about the origins of the data.*

*I regard it as unethical for a statistician not to have asked questions about the origins of anomalies in data such as I have described, but I hesitate to be condemnatory about a young statistician, aged perhaps 24, who had probably never been taught differently."*

I would be not only surprised if this experience does not bring out some reaction from the ISCB members, at least those employed by the pharmaceutical industry.

Mats Lörstadius  
ISCB-News Editor  
AB Hässle  
S-431 83 Mölndal  
Sweden



**BRUSSELS 1991: JOINT MEETING WITH THE SOCIETY FOR CLINICAL TRIALS - INTENTIONS, PLANS AND PROGRESS REPORT.**

Plans are progressing well for this meeting, to be held from 8-12 July 1991 at the University Hospital St Luc, Brussels, Belgium, under the High Patronage of His Majesty the King of Belgium. All sessions will be joint between the two societies, ISCB and SCT, with common registration and reservation procedures. A Programme Committee will be formed, under the joint chairmanship of Curt Furberg (SCT) and Stuart Pocock (ISCB), and details of the programme will be available within the next few months. The final day may be devoted to courses and one half-day is likely to be scheduled for a workshop or minisymposium. The Local Organizing Committee, under the chair of Marc Buyse, has been active since September 1989, and we can look forward to an exciting conference combining the interests and talents of both societies. The formal First Announcement should appear during the coming summer, and I hope there will be a big response from both sides of the Atlantic.

Peter Armitage  
ISCB Vice-President

**TOWARDS 1991, PROGRESS REPORT.**

To ISCB, 1991 will be a special year because for the first time ISCB will join forces with the Society for Clinical Trials (SCT) for a joint meeting.

Preparations started many months ago. The local organizing committee, has now held four official meetings and many problems have been discussed, resolved or are in the process of finding a resolution, from air travel to ground transport, academic sessions to social activities (most importantly, ed.), the format of the meetings to stationery and logo, budget, funding, hotels, publicity, etc.

Of course, the job is not made any easier by having to communicate across the Atlantic.

A meeting was held in London in early April to take stock of the situation. On the ISCB side the President Wolfgang Köpcke, Secretary Jorgen Seldrup and Treasurer Douglas Wilson together with the Vice-President Peter Armitage met with PC Chairman Stuart Pocock. Several important issues were discussed relating for example to the constitution of the Programme

Committee, Meeting topics, Programme structure, Courses in connection with the meeting, Finance and Communication. The views of the meeting will be discussed in Toronto in early May at the SCT meeting. And the preparations go on and we are confident that we can all look forward to a grand meeting, the coming together of two societies with a common interest in medical statistics.

We look forward to seeing you all in Brussels, 1991. But, of course, first we hope to see you in Nimes, France, September, 18-21, 1990.

Jørgen Seldrup

**Clippings:**

It is of particular interest to ISCB members to note that all three of the prestigious Guy Medals awarded in 1990 went to statisticians active in the area of biostatistics. In particular attention is drawn to the recipient of the Gold medal. The ISCB congratulates its Vice-President.

**ROYAL STATISTICAL SOCIETY NEWS & NOTES, APRIL 1990**

**Society Medals**

**The Guy Medal in Gold** for 1990 will be awarded to Professor P Armitage for his outstanding contributions to the theory and practice of statistics within the medical field and elsewhere; for his pioneering introduction of sequential analysis into clinical trials; for his educational work in improving the quality of the design and analysis of clinical trials and other medical research; for his extensive work on specific medical problems; and for his many contributions to statistics generally.

**The Guy Medal in Silver** for 1990 will be awarded to Mr D G Clayton for his paper (with J M Cuzick) on "Multivariate Generalisations of the Proportional Hazards Model" read to the Society on 13 February 1985 (JRSS A 148 82-117) and for his varied publications in "Applied Statistics", taking into account his imaginative contributions to GLIM and his innovative work on complex epidemiological modelling.

**The Guy Medal in Bronze** for 1990 will be awarded to Dr V S Isham for her paper on "Mathematical Modelling of the Transmission Dynamics of HIV Infection and AIDS: a Review" read to the Society on 25 November 1987 (JRSS A 151 5-30 and 120-123).