



International Society for Clinical Biostatistics

Number 2 January 1986

Editor: J. Seldrup

Again!

Yes, I am happy to announce our second Newsletter. Judging from the response and the kind letters I have had, you seem to have enjoyed our new 'innovation' (although I hate to think what the selection bias is like).

So, due to popular demand, we will also send this second issue of the newsletter to everyone on our mailing list. However do consider taking out membership and ensure the receipt of future newsletters.

We have a new chairman of the Society, Douglas W. Wilson of the Tenovus Institute for Cancer Research. You will find a profile of him below. Over the page the leader is on Pooling. You will also find a 'letter to the editor' regarding

adverse drug reaction monitoring, a report of the 4th Executive Committee meeting, an invitation to come to Cardiff for ISCB-7 in September 1986, and the concluding chapter of the history of the Society, together with 'regulars' - the 'letter home from . . .' and a meetings diary.

Profile



D.W. Wilson

The 1985/86 President of the Society for Clinical Biostatistics, Douglas W. Wilson, was born in England in July 1940, but moved at an early age to Wales, where he received his primary, grammar school and university education. He obtained his Ph.D. from the University of Wales.

Since his initial appointment at the Tenovus Institute for Cancer Research, Cardiff in 1966, he has for the past ten years been Head of the Statistics, Computing and Chronobiology Unit. Special interests include Quality Control, Time Series Analysis and Prognostic Index Models and their relevance and application to problems related to endocrine cancer research.

His professional activities include being Chairman of the British Society for Chronobiology, Council Member of the International Society for Research on Civilization Diseases and Environment, Fellow of the Royal Statistical Society and the Institute of Statisticians and a Member of the British Computer Society. His hobbies include sport and the promotion of science among the lay community through the Cardiff Scientific Society of which he is Chairman.

Executive Committee 1985 / 86

President

Dr. D.W. Wilson (Cardiff)

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Professor G. Gallus (Milan)

Co-option

(Immediate past President)

Professor H.J. Jesdinsky (Düsseldorf)

Croeso i Cymru

15 - 19 September

Come to Cardiff

Welcome to Wales

1986

See page 5 for details

Pooling or Meta-Analysis

In recent years there has been a growing interest in combining the results in a formal (objective) way of research experiments in the social and health/medical fields. Many articles and several books now address the subject of pooling, i.e. summarising data - often referred to as Meta-Analysis. Of course, medical researchers have used less formal methods for many years: literature surveys, review of published/unpublished material or even graphical displays. No medical publication is without a discussion of 'the results' in relation to existing knowledge, beliefs or practice.

There is frequent debate about the wisdom of applying formal statistical methods in combining results of often heterogenous studies. However, the arguments may equally well apply to less formal methods.

The biggest danger probably lies in the bias introduced by the selection of studies for pooling. Whether a combination of results are sought for a certain therapy or a medical condition it must be decided which study results to use. It ought to be relatively simple to obtain access to published results but what about unpublished results? These will tend to be 'negative' either because researchers or journals are less than enthusiastic about publishing unexciting results. Even if we assume (or indeed verify) that all results relevant to our hypothesis are available many other aspects must be addressed before pooling.

Should we only use randomised trials? Should they be a certain size? Does the quality vary? Were the study protocols different (subjects, diagnosis, dosage or dosage forms, response variables, treatments, design) ?

When all is said and done it is unlikely that any sophisticated pooling technique can ever be a substitute for well designed, planned and executed research, although it may well have a place alongside it.

History of ISCB Part 2

Part 1 appeared in ISCB NEWS Number 1, July 1985, describing the history up to ISCB-3, 1982.

ISCB-3 took place at the Erasmus University in Rotterdam, the local organising committee being chaired by Professor R. van Strick. A special feature of the meeting was a mini-symposium on Prediction of Survival in Cancer. This kind of event was to become a feature of future ISCB meetings.

It was at a General Meeting in the Erasmus University on 14th September, 1982, that a formal Executive Committee was formed, based on a constitution submitted to and accepted by members of the Society present at the Meeting. The inaugural president was Professor E. Marubini.

The following meeting of the Society, ISCB-4, was held in Paris during September 1983 thanks to Dr. H. Sancho-Garnier and her team from Villejuif. The one day symposium this time was on Diabetes. At the AGM that year Professor R. van Strick was elected president of the Society.

The fifth meeting of the Society, ISCB-5, took place in San Marino in

September 1984, organised locally by Professor E. Marubini. This meeting set in beautiful surroundings of this historic republic, continued to maintain the high standard in clinical biostatistics established at previous meetings. The well attended meeting included a mini-symposium on Gastroenterology dealing with the development of methods of analysis concerned with the natural history of digestive disorders and the evaluation of digestive tests in gastroenterology. At the AGM that year Professor H. Jesdinsky (Düsseldorf) was elected president of the society.

Last year ISCB joined forces for the first time with another society (GMDS, Deutsche Gesellschaft für Medizinische Dokumentation, Informatik und Statistik) to put on ISCB-6 in Düsseldorf, the mini-symposium this time being on Clinical Oncology. Dr. D.W. Wil (Cardiff) was elected president at the AGM.

This concludes the history of a yet very young Society. Judging from the support we have had over the years at our annual meetings, we believe we have got a role to play - that we fulfill a need. Continue to support us, not just by attending our meetings but by taking out membership as well, and you will help us to help you to plan for the future, not just for the sake of the Society, but through it for our aims and ideals.

Letter home from Düsseldorf

Dear All

It is the last day of the ISCB-6 Conference. I have just had my lunch, and I am sitting outside what looks more like a concrete bunker than a lecture theatre. But I must not be unkind. In the sunshine, and we have had a fair amount of that in the last couple of days, although it was a bit drab, when we arrived, this place looks quite alright. As for the City, this has been a pleasant surprise. Life in 'Altstadt' in particular was pleasant and it offered a good chance to practice my German. Although one night I got a bit stuck when approached by a young lady, who wondered where we could go for a quiet drink, initially. However, I did manage to tell her that I did not know, and in any case I was going back to my hotel, as I had to be up bright and early to chair a session in a conference of biostatisticians. I am not sure she understood the last bit.

The Germans certainly did themselves proud with their organisation of lunch. You bought a ticket in advance for a particular set meal, queued up in the relevant place, and there, 'hey presto' appeared the entire meal on a tray. I still don't like sauerkraut. And they had an affinity for numbering everything. For example, did you know that 21.0 0.82.1 was the little boy's room in Neue Mensa - the staff restaurant building. Not only that, but in 21.0 0.82.1 you could actually sit down and do it.

I almost did not get to the conference on time the first morning. On enquiring at the hotel I was told the wrong tram, and pointed in the opposite direction of the university. No, it was not my German failing me, but it could have been the receptionist's English failing her. I never did work out why the trams were numbered from 600, the roadsweepers from 500, the public garden mowers from 400 . . . and that is without any decimal points.

I must go now, but before I do, I must tell you about the lovely party I went to last night at the President's house (no, not Herr Kohl's). The weather was mild, the food was beautiful and the wine uncontaminated.

Kind Regards J.S.

International Society for Clinical Biostatistics 1986 Membership Application

New members only: existing members will be invoiced

I wish to subscribe to ISCB as follows (tick one box):

- £10 Ordinary membership of ISCB to 31 December 1986
- £5 Full-time student membership of ISCB to 31 December 1986
- £49.50 Ordinary membership of ISCB to 31 December 1986
plus
1986 UK subscription to 'Statistics in Medicine'
(Note: UK only; elsewhere higher rate shown below applies)
- £57.50 Ordinary membership of ISCB to 31 December 1986
plus
1986 overseas subscription to 'Statistics in Medicine'

I understand that this fee, if paid by 28 February, 1986, entitles me to a discount of £15 on the registration fee for the 1986 meeting of ISCB in Cardiff.

Surname _____

Initials _____

Title (Professor/Dr/Mr etc) _____

Post held _____

Business address in full _____

Post code and country _____

Please state whether you trained as a statistician or as a doctor (medically qualified, that is a physician/surgeon) and also whether you now work as a statistician or as a doctor

	By training (tick one box)	By present occupation (tick one box)
Statistician	<input type="checkbox"/>	<input type="checkbox"/>
'Doctor'	<input type="checkbox"/>	<input type="checkbox"/>
Both	<input type="checkbox"/>	<input type="checkbox"/>
Neither	<input type="checkbox"/>	<input type="checkbox"/>

The following cheques, made payable to 'The International Society for Clinical Biostatistics' are acceptable:

a British bank cheque a Sterling Eurocheque any cheque drawn in sterling and payable in London (on a named London bank)

Payment as above (tick one box)

is enclosed will follow under separate cover

Signed _____

Date _____

Please forward to the Honorary Treasurer:

Dr W Koepcke,
Biometric Centre for Therapeutic Studies,
Pettenkofer Str. 35,
800 München 2,
FR-Germany

International Statistical Institute (ISI)

Report on Meeting of Presidents of Statistical Societies August 16, 1985 (shortened)

During the Centenary Session of the International Statistical Institute, in August 1985, in Amsterdam, the Netherlands, the ISI organised an informal meeting of Presidents of national and international statistical societies.

The purpose of the meeting was to explore methods through which the societies could increase mutual co-operation.

Societies represented at the meeting were:

International Statistical Institute	Inter American Statistical Institute
American Statistical Association	International Association for Statistical Computing
Association des Statisticiens Universitaires (France)	International Association of Survey Statisticians
Bernoulli Society for Mathematical Statistics and Probability	Israel Statistical Association
Biometric Society	Italian Society of Statistics
Egyptian Statistical Association	Japan Statistical Society
Federation of Statistical Societies of Yugoslavia	National Statistical Society of China
Institute of Mathematical Statistics	Netherlands Society for Statistics and Operations Research
Institute of Statisticians (UK)	Société de Statistique de France
International Union for the Scientific Study of Population	State Institute of Statistics Turkey

During discussion the participants addressed the following issues:

- promotion of understanding and use of statistics within countries, including recruitment of students to the profession, informing the general public and educating the young;
- regional co-operation including the organisation of regional meetings in developing countries;
- co-operation and exchange of information between societies, including the routine exchange of newsletters and co-operative participation in conferences;
- the impact of computers in statistics and relations between statistical societies and computing societies;
- codes of conduct within countries and the ISI Declaration on Professional Ethics.

As a result of these discussions it was agreed that a second meeting of Presidents should be held in September 1987, during the 46th ISI Session in Tokyo, Japan. Organisation of the meeting is at a preliminary stage, but further details will be circulated to all societies listed in the ISI Directory. However, topics for discussion may include: an exploration of

the relationship between ISI and individual national societies and regional societies, and the development of means to improve this; the encouragement of the creation and growth of national societies, particularly in developing countries; the development of ways to encourage closer relations between national societies to their mutual benefit.

The International Statistical Institute welcomes the anticipated co-operation of societies in the envisaged development of these closer ties.

Further details from:
International Statistical Institute
428 Prinses Beatrixlaan
PO Box 950
2270 AZ Voorburg
Netherlands

Letter to the Editor

Dear Editor,

I thoroughly enjoyed your newsletter, so much so that I am now thinking of joining the ISCB in order to continue receiving it. I was especially interested in your leader on Adverse Drug Reactions (ADRs) because I was beginning to think that the ISCB was simply a clinical trial society.

You say that epidemiologists and statisticians have much to contribute to post-marketing surveillance (PMS). As one of very few statisticians involved full-time in PMS, I agree, although I believe that it is unlikely that statisticians within the pharmaceutical industry will have the opportunity to become more involved in PMS studies.

In my opinion statisticians do have a part to play in drug epidemiology, not in the pharmaceutical industry, but in independent units such as the Drug Surveillance Research Unit (DSRU). However, the role is not the traditional one of a statistician. It has been compared with that of a Roman augur (1), but Finney's (2) comparison with the role of a detective is a much better one.

Finney was writing about the statistician's role in drug monitoring systems, such as the CSM's 'yellow card' system or the DSRU's Prescription-Event Monitoring (PEM). These systems generate hypotheses, unlike cohort and case-control studies which are primarily hypothesis testing techniques. In these hypothesis generating systems, the data have often not been collected according to ideal statistical principles. This presents a challenge to statisticians. As Finney has pointed out on several occasions, if we refuse to soil our hands with such 'dirty data', we are agreeing, by default, that the interpretation should be left entirely to non-statisticians.

You suggest we should debate a practical solution to PMS. Since the thalidomide tragedy hundreds of meetings have discussed PMS and many techniques have been proposed, but few practical results have been achieved. Over the last five years I have been associated with PEM, which is one of the very few innovations that have been put into practice. While it is not the ultimate PMS technique (if there is such a thing), PEM is now an established, practical and useful method for monitoring adverse reactions to new chemical entities used in general practice (3).

The whole issue of ADRs is of course confounded by how society perceives risk and how this perception is influenced by the media. The risk of death or disability when driving a car is acceptable, but the very much lower risks of serious or fatal adverse reactions to drugs appear to be unacceptable. Many factors must be taken into account when evaluating the risk-benefit ratio. However, only when society can assess and compare risks without being heavily influenced by either its own misconceptions or the media will it be possible to design the most suitable PMS studies and establish risk-benefit ratios (4). Statisticians working in PMS must be not only augurs or detectives but also teachers attempting to put the risk of ADRs into context.

N.S.B. Rawson
DSRU, Southampton, UK

References

- (1) Johnson, A.F. Post-marketing surveillance: statistics and augury. *J Chron Dis* 1984; 37: 949-952.
- (2) Finney, D.J. Statistical aspects of monitoring for dangers in drug therapy. *Methods Inf Med* 1971; 10: 1-8.
- (3) Inman, W.H.W., Rawson, N.S.B. Prescription-Event Monitoring of five non-steroidal anti-inflammatory drugs. In: Rainsford, K.D., Velo, G.P., eds. *Side Effects of Anti-Inflammatory Analgesic Drugs*. Boca Raton, Florida: CRC Press (1986, in press).
- (4) Inman, W.H.W., Risks in medical intervention: balancing therapeutic risks and benefits. In: Cooper, M.G., ed. *Risk: Man-made Hazards to Man*. Oxford: Oxford University Press, 1985; 35-53.

Come to Cardiff 15-19 September 1986

Tenovus Institute for Cancer Research at the Welsh National School of Medicine will host the Seventh Meeting of the ISCB, 15-19 September, 1986, in Cardiff, the Capital City of Wales.

Whilst the meeting proper starts on Tuesday, following a civic reception at the City Hall on Monday evening, it is hoped that a short course on clinical trials can be arranged as a satellite meeting on the Monday.

This introductory course, for which there will be a separate charge, may be followed by a more advanced course, probably as a parallel session to the main meeting.

The Law Building of University College, Cardiff, the venue of ISCB-7, is next to Cathays Park near the centre of the city, the newly opened shopping area of St. David's and the nearby Cardiff Castle with its 1900 years of History.

For rugby fans a trip to Cardiff may be a pilgrimage, the music lover may enjoy a concert in St. David's Hall or the Welsh National Opera at the New Theatre, poets will want to visit 'Under Milk Wood'.

Amser da yu Caerdydd.

ISCB-7 Caerdydd (Cardiff) 15 - 19 September, 1986

The main themes of the Conference will be:

- A Clinical trial methodology**
reasons for stopping; survival analysis; use of historical controls
- B Quality assessment in health care**
role of quality control in laboratory medicine; surveillance of health events or clinical audit; comparative studies
- C Statistical modelling in medicine**
stochastic models in biomedicine; natural history of disease; time series; clinical usefulness of pharmacokinetics
- D Assessment of complementary (alternative) medicine**
methods and problems of evaluation
- E Mini-symposium on human prostatic disease**
in collaboration with the British Prostate Study Group
- F Workshop on statistical consulting and teaching of biostatistics in medical schools**
including a report from UK medical school statisticians
- G Assessment of risk factors and prognosis**
post-marketing surveillance; measurement of risk; methods of clinical epidemiology



Report of 4th Executive Committee Meeting

The Executive Committee held its 4th meeting, the chair being taken by the President, Dr. D.W. Wilson, at the University of Düsseldorf at the end of ISCB-6.

The minutes of the previous meeting were signed as a correct record. One of the matters arising was the possibility of awarding a prize for the best presentation. It was thought that this would be too difficult to judge, but the possibility of a prize for the best published paper in the editorial proceedings would be given further consideration. A short course on clinical trials in connection with ISCB-7 was discussed. The possibility of an introductory course immediately preceding ISCB-7, and a more advanced course as a parallel session(s) is being pursued by the local organisers.

In accordance with the recommendation from the Society's General Meeting held the day before, it was agreed:

(a) to co-opt the retiring President, and
(b) to recommend to the next General Meeting a change in the rules to allow the President of the day to serve as an ex-officio member of the Committee for an additional year.

The treasurer reported on the accounts of the San Marino meeting which were at one stage in danger of being in deficit. Additional sponsorship however, had resulted in a break-even situation. The finances of the Düsseldorf meeting were naturally not yet sorted out, but Professor Jesdinsky reported that the social programme was likely to make a loss, whilst income and expenditure for the scientific programme were likely to be similar. The Meeting, which had a common budget for the whole of PROMED WOCHEN, had received substantial grants from both the Federal Government and the government of the North Rhine Westphalia.

The treasurer's provisional report for the first six months of the financial year showed that income exceeded expenditure and that cash in the bank amounted to £10,375 (approximately 41,500 DM).

As discussed the day before at the General Meeting, it was agreed to accept an invitation from Dr. Lörstad to hold the ISCB-8 in Gothenburg in 1987, subject to final agreement. Further future venues, Basel and Geneva, were discussed, as was the possibility of joint meetings with the Society of Clinical Investigations and the Society for Controlled Clinical Trials, but no firm decisions were made.

It was agreed that the link with the Operational Research Society, the Indian Society for Medical Statistics and the Association Columbiana de Estadísticos should be a reciprocal arrangement of announcement of activities. Proposals for a joint meeting with the Indian Society for Medical Statistics in India and one with the University of Khartoum in Sudan were declined. It was hoped however, that ISCB in general could encourage links with related national societies including those of the Eastern Bloc countries.

It was confirmed that ISCB-7 would take place in Cardiff in 1986 (see page 5 of this newsletter for further details).

It was reported that the first issue (July 1985) of the ISCB Newsletter had been mailed to about 1600 addresses on the mailing list.

The meeting closed just after 8pm.

Be sure to receive future newsletters

BECOME A MEMBER OF ISCB
International Society for Clinical Biostatistics

Support our aim to stimulate research on the principles and methodology in the design and analysis of clinical research, to increase the relevance of statistical theory to the real world of clinical medicine; and, through scientific meetings to create an opportunity for the exchange of knowledge, experience and ideas among clinicians, statisticians and members of other disciplines (e.g. epidemiologists, clinical chemists and clinical pharmacologists) working in, or interested in, the field of clinical biostatistics.

For only £10 you may take out ordinary membership, and get a £15 discount on the registration fee for the meeting in Cardiff, (provided the subscription is paid by 28th February, 1986) - the fastest way yet known to statisticians to make a profit of 50%. But the 'Goodies' do not finish here. If, at the same time, you take out a subscription to 'Statistics in Medicine', this will only cost you an additional £39.50, if you live in the UK (as against the ordinary subscription rate of £79) and £47.50 elsewhere (as against the ordinary rate of \$145, just over £100, although dependent on exchange rates).

For application of membership (new members only - existing members will be invoiced) see the middle page of this newsletter or contact the Honorary Secretary.

Correspondence for, or about, the newsletter should be sent to

Dr. J. Selstrup
Ciba-Geigy Pharmaceuticals,
Wimblehurst Road, Horsham, West Sussex.
RH12 4AB United Kingdom.

Other enquiries, for instance about membership should be sent to

Dr. R.A. Dixon
University of Sheffield Medical School,
Beech Hill Road, Sheffield,
S10 2RX United Kingdom.

1986 Calendar

February 5-7

**Qualitative Methods of Research:
A Matter of Interpretation**

Amsterdam, The Netherlands
Contact: ESOMAR Central Secretariat,
JJ Viottastraat 29, 1071 JB Amsterdam,
The Netherlands.

February 9-12

**The future of Adverse Drug Reactions:
Computers, Clinical Judgement and the
Logic of Uncertainty**

Arlington, Virginia, USA
Contact: Drug Information Association,
PO Box 113, Maple Glen, PA 19002, USA

February 20-26

Foundation Course in Clinical Trials

London, UK
Contact: Clinical Research Services Ltd.,
36 Neald Crescent, London, NW4 3RR, UK.

February 25 - 28

**Epidemiological Approaches to Achieve
Health for All**

Maharani Laxmi Bai Medical College,
Jhansi (U.P.), India
Contact: Professor R.N. Srivastava,
I.E.A. Regional Scientific Meeting,
Dept. of Social and Preventive Medicine,
M.L.B. Medical College, Jhansi - 284 128, India

February 27 - March 1

**International Monica (Monitoring of Trends
and Determinants in Cardiovascular Diseases)
Congress**

Augsburg, FRG
Contact: GSF München, Kongress-Dienst,
Ingolstädter Landstrasse 1, D-8042 Neuherberg,
Federal Republic of Germany

April 6-9

**Joint Meeting of British and Nordic Regions
(Biometric Society)**

Churchill College, Cambridge, UK
Contact: Mr D. Brown, Biometric Conference,
AFRC Statistics Group, Dept. of Applied
Biology, Pembroke Street, Cambridge,
CB2 3DX, UK

April 7-11

**Fourth Sheffield Conference on Influential
Data Analysis**

University of Sheffield, UK
Contact: Conference Secretary, Dept. of
Probability and Statistics, University of
Sheffield, Sheffield, S3 7RH, UK

May 11-14

Society for Clinical Trials - 7th Annual Meeting

Montreal, Canada
Contact: Mary A. Finch, Meeting Co-ordinator,
Society for Clinical Trials, Inc., 600 Wyndhurst
Avenue, Baltimore, Maryland 21210, USA

June 10-13

**International Association for Regional and
Urban Statistics, 15th General Conference**

Innsbruck, Austria
Contact: ISI Permanent Office, 428 Prinses
Beatrixlaan, PO Box 950, 2270 AZ Voorburg,
The Netherlands

June 16-19

European Organisation for Quality Control

Stockholm, Sweden
Contact: The Swedish Association for Quality,
Box 5884, S-102 48 Stockholm, Sweden

July 8-11

Practical Bayesian Statistics

Cambridge, UK
Contact: The Conference Secretary,
The Institute of Statisticians, 36 Churchgate
Street, Bury St. Edmunds, Suffolk,
IP33 1RD, UK

July 26 - August 1

**III World Conference on Clinical
Pharmacology and Therapeutics**

Stockholm, Sweden
Contact: CPT-86, c/o Stockholm
Convention Bureau, Box 1617, S-111 86
Stockholm, Sweden.