

International Society for Clinical Biostatistics

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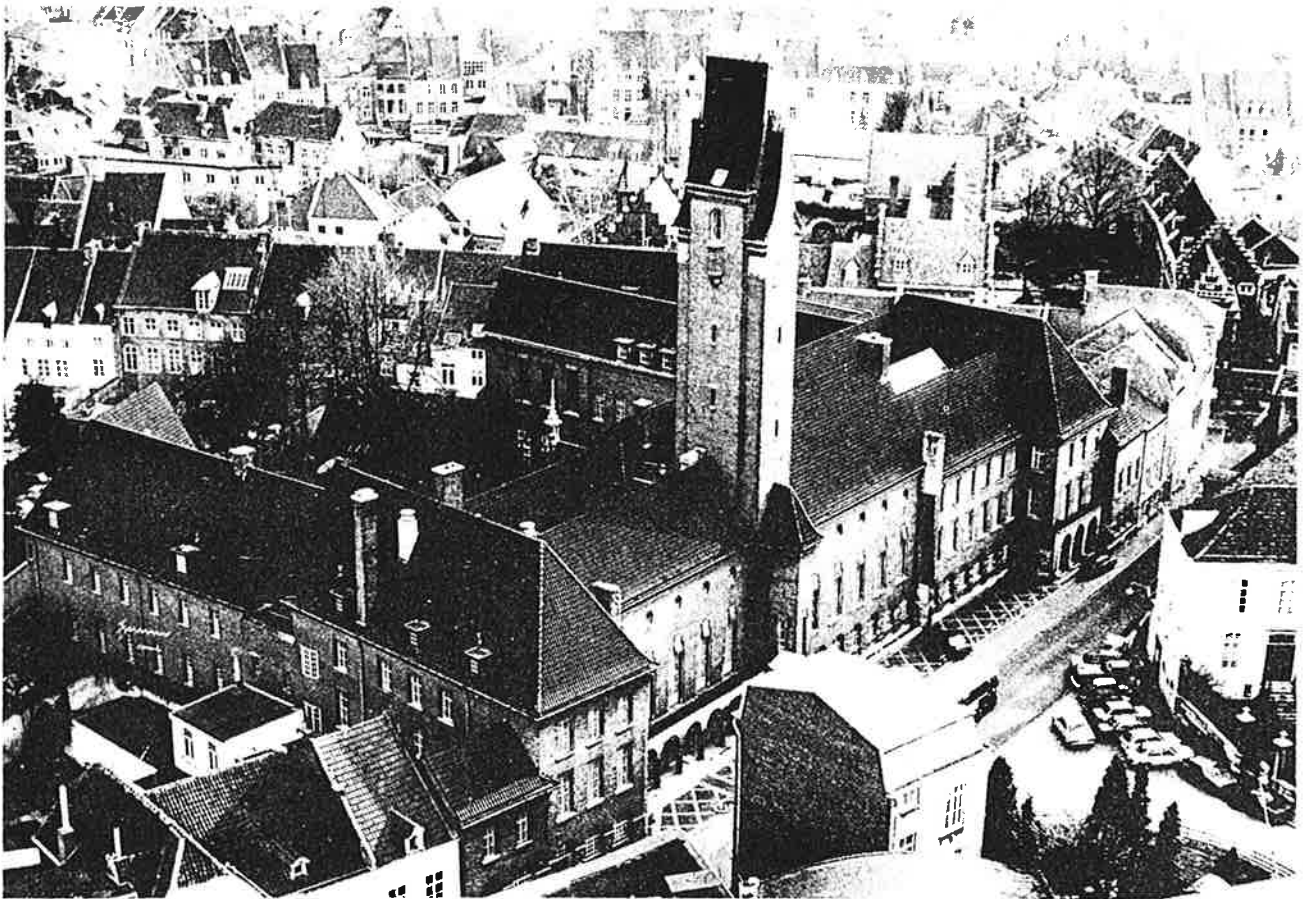
Number 6

May 1989

Editor : D.W.Wilson

WELCOME TO MAASTRICHT ON OUR TENTH ANNIVERSARY

(September 11th to 14th inclusive, 1989)



It is most fitting that our tenth anniversary is to be held in The Netherlands. Those of you who joined the Society many years ago will remember that The Netherlands hosted the first fully constitutionalized Meeting of the Society in Rotterdam in 1982. The Local Organizing Committee for ISCB-3 in Rotterdam, in many ways, set the high standard of ISCB Meetings that we now expect. It must also be remembered that many, each in their different way, have forged milestones in ISCB history. Already, there are early signs that the Maastricht Meeting (ISCB-10) is well on course to becoming yet another superb event.

Maastricht is a pleasant old town in the south of The Netherlands, situated in green hills and nearby Belgium and West Germany. Due to its rich and long history Maastricht is one of the most beautiful cities in The Netherlands with medieval churches, houses and streets.

The host institution will be the University of Limburg. This University was founded in 1976 and has schools of Economics, Law and Medicine and Faculties of Health Sciences and General Sciences. The University is steadily growing to an expected 6,000 students in 1990.

All the sessions of the 10-th meeting will be held in the Maastricht Exhibition and Congress Centre (MECC). The MECC is an ultra modern centre for conventions. Accommodation will be provided in Maastricht and its immediate surroundings.

The picture seen on this frontispiece centres on the 'Oud Gouvernement' building located at 23 Bouillonstraat 3, Maastricht which is the administration block of the University of Limburg and where participants at ISCB-10 will register and be welcomed by Dr Ronald Does and his team. The Local Organising Committee and the Chairman of the Programme Committee have worked diligently to bring Members of the Society a first class Meeting combining professionalism at the highest level with opportunities for social interaction. The programme themes are listed overleaf but readers of this Newsletter are asked to support Ronald Does and his team by advertising the Meeting and influencing colleagues to participate. Batches of Newsletters are available and will be sent to those who would like to distribute them for the ISCB.

On behalf of Dr Does - Welcome to Maastricht.

ISCB-10 Scientific Programme

The main objectives of ISCB meetings is to create an opportunity for the exchange of knowledge, experience and ideas between clinicians, statisticians and members of other disciplines, like epidemiologists, clinical chemists, clinical nutritionists and clinical pharmacologists, working in or interested in the field of clinical biostatistics. The session themes, invited speakers and (provisional) titles for the tenth meeting are :

Clinical Trials

- J.P. Boissel (F)
A. Heyting (NL)
S.J. Pocock (UK)
M. Zelen (USA)
- Surrogate end-points in clinical trials: need for theory.
 - Statistical handling of drop-outs in clinical studies.
 - Estimation problems in clinical trials and overviews.
 - The role of non-compliance in the planning and analysis of clinical trials.

Epidemiology

- A.J. Valleron (F)
J.P. Vandenbroucke (NL)
- AIDS Epidemiology in France : trends and short-term predictions.
 - The clay feet of today's epidemiology.

Statistical Modelling

- J.C. van Houwelingen (NL)
D. Oakes (USA)
- Predictive value of statistical models.
 - Appropriate and inappropriate uses of compliance data in the analysis of randomized clinical trials.

Survival Analysis

- W. Albers (NL)
D. Clayton (UK)
- Comparing survival curves using rank tests.
 - A Monte Carlo approach to random effect models in event history analysis.

Medical Decision Making

- F.T. de Dombal (UK)
J.D.F. Habbema (NL)
J. Hilden (DK)
Ch. Ohmann (FRG)
- Practical problems in providing computer aided decision support.
 - On comparing the performance of diagnostic tests.
 - The marriage of clinical trials and clinical decision science.
 - Clinical impact of medical decision making in upper gastrointestinal bleeding.

General Aspects of Clinical Biostatistics

- D.J. Finney (UK)
G. Beaton (CDN)
- Statistical science beyond the textbook.
 - To be announced.

Minisymposium on Nutrition

- F. ten Hoor (NL)
J.R. Speakman (USA)
P. Webb (UK)
K.R. Westerterp (NL)
- To be announced.
 - The doubly labelled water technique : principles, current issues and a paradox.
 - Variability of 24-hour energy expenditure and other quantities.
 - Variation in fat-free mass of the body explained from fatmass and habitual activity level.

An ISCB course on Clinical Trials is also scheduled for Friday the 15th of September 1989. For further details of ISCB-10, please write to Conference Secretariat (ISCB-10), Department of Medical Informatics and Statistics, University of Limburg, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

Scientific programme committee (ISCB-10)

Chairman : R. van Strik (The Netherlands)
C.P. Chastang (France)
R.J.M.M. Does (The Netherlands)
G. Gallus (Italy)
E.A. Gehan (U.S.A.)
A. Hasman (The Netherlands)
W. Koepcke (FR-Germany)

M. Lörstad (Sweden)
A. Neiss (Austria)
F. ten Hoor (The Netherlands)
J.C. van Houwelingen (The Netherlands)
D.W. Wilson (United Kingdom)

Local organizing committee (ISCB-10)

Chairman : R.J.M.M. Does
Secretary : F.H. Hein
Members : A. Bronkhorst A.D.M. Kester M.H.A. Vanherle

Vice-chairman : H.J.A. Schouten
Treasurer : M.P.E. Janssen



**ISCB President 1988/89
DR. Mats Lörstad**

Dr. Lörstad was born in 1938 under the sign of Pisces. He began academic life by enrolling at the University of Lund in 1958 where he obtained his first academic degree in 1963 in statistics, mathematics, sociology and pedagogics. He was then employed as a teacher at the University in the Department of Statistics. During this time he met his wife, Ulla-Britt, and they have three sons. In 1967, he went on to receive his PhD for work on sampling theory and applications. Employed by the Statistics Division of the UN Food and Agriculture Organization (FAO), Rome, Italy as a Statistician with the Social Statistics Section (1968), Mats was later transferred to the Nutrition Division as Nutrition Officer, to work with statistical problems in nutrition studies, in particular Food Consumption Surveys. In 1971 he had a field assignment with the National Food and Nutrition Programme in Lusaka, Zambia as Chief Methodologist and subsequently Project Manager. He later returned to the FAO to become responsible for FAO Nutrition Division as consulting support to nutrition-related surveys in Asia and Eastern Africa. In 1977 he returned to Sweden to be self-employed, working as consulting statistician to FAO and other international organizations, and was particularly concerned with the development of computer systems in Sweden.

In 1981 he was employed as Section Manager at Hässle, Mölndal to establish a Section for Medical Data Management. This has now grown to become the Dept. of Medical Statistics and Data Management.

Dr. Lörstad's interests are now mainly concerned with the development of management nature : how efficient communication between statisticians and

applied research within his Company can be achieved. His work for the ISCB is known only too well and his hobbies include music (Italian opera), cooking (Italian, of course) and golf. In his year of Office, Dr. Mats Lörstad has been active in promoting ISCB at every opportunity, particularly with negotiations with the EORTC on the planning of a future event with them and the Society for Clinical Trials.

LETTERS

Dear Dr. Wilson,

As you are aware, the Institute of Statisticians has established a consultancy company which may be of interest to Members of the ISCB, who may wish to participate by offering their services so as to fulfil contracts as they arise. I submit an extract from publicity material which your readers may find interesting : -

IoS Consultants Limited is a company which is wholly owned by the Institute of Statisticians: a professional body which is obliged in the public interest to provide the best possible statistical service and advice. The Institute of Statisticians has published a Code of Conduct to which all statistical consultants acting on behalf of IoS Consultants Limited are fully committed. The aims of IoS Consultants Limited are to :

- make available to all education and health services, internationally, the benefits of statistical methodology;
- establish and maintain high qualities of statistical consultancy.

IoS Consultants Limited is in touch with several hundred professional statisticians whose qualifications and experiences are documented. Some of these are available for only brief periods of a few days, while others are available for long-term contracts. The areas of application in which they are experienced are widely varied. Teams of consultants can be convened when clients require extra support

Perhaps, at your ISCB Meeting following Maastricht, your Members may appreciate a small section on the topic of Consultancy in Medical Statistics. Perhaps some of your readers would like to express their opinions on this matter through your Newsletter.

Tony Greenfield,
Institute of Statisticians,
50 Fitzroy Street,
London W1P 5HS

A LETTER HOME FROM INNSBRUCK

Dear friends and colleagues,

It is the last day of the ISCB-9 conference and I am sitting on the balcony of the conference centre, drinking coffee and admiring the view of the mountains around Innsbruck. There is snow on the mountains. It came during our visit, although it fell as rain here in the valley. It has rained on several days but I have, nevertheless, enjoyed my time in Innsbruck. The old town is fascinating with tall elaborately painted buildings and shops set back in vaulted arcades. The fast-flowing river Inn runs around the edge of the old town and towering over it all are the mountains. The focal point of Innsbruck is the 'Golden Roof', which is an ornate balcony sheltered by a roof of golden tiles, built in 1500 as a royal box from which to watch events held in the square below. Today, any royal visitors would look down on and smell a mobile burger bar parked directly beneath them!

What about the conference that is supposed to be the purpose of my visit, I can hear you say. Well, like most conferences, this one has had good, bad and indifferent parts. Sadly, some of the most tedious papers have been given by invited speakers, but these have been a minority and have been outweighed by some stimulating contributed papers. The most entertaining speakers have, of course, been the Bayesians. Do Bayesians develop their style as a kind of shield to protect themselves against the onslaught of the frequentist majority or is it simply that natural extroverts tend to become Bayesians? The conference has mainly been organized in four parallel sessions and, therefore, one has either had no choice in what to attend or had to be very selective, rushing from one lecture room to another every 20 minutes or so. Inevitably, there have been times when I wanted to be in two places at once. Also, since I often seemed to be in the room with the smaller audience and the hard seats, I assume I must have minority interests. The mini-symposium was on 'Quality of Life', but I am still no wiser as to what this term actually means.

I attended my first Annual General Meeting of the ISCB yesterday. It was sandwiched between the last session of the day and the departure for the annual dinner, the time when many people were taking a shower and having a drink to recover from the day to prepare for the evening binge. Consequently, there were so few ordinary members attending that the committee members almost outnumbered them. The meeting

lasted for nearly two hours! It could have been shorter if committee members indulged in less mutual admiration and there were fewer time-wasting calls for votes of thanks and appreciation. The meeting was, nevertheless, entertaining. For instance, there were repeated demands from one member for the officers of the Society to speak up and, when they failed to do so, they were each given a pen and an overhead projector slide to write their words down. On a more serious point, the ISCB has, in the past, appeared to me to be primarily a society for clinical triallists and at the meeting it was proposed that the ISCB-12 conference should be held jointly with an American clinical trials society. This proposal was not greeted with unanimous enthusiasm and it led to demands from ordinary members for a widening of the aims of the ISCB rather than apparent narrowing of them.

I can hear the dreadful warbling sound, like car alarm, which signals the beginning of the final session and so I must go. Before I do, I can tell you that the next meeting will be held in Maastricht - wherever that is!

Nigel Rawson
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The Institute of Cancer Research
Belmont, Surrey, SM2 5NG

ISCB Hon. Secretary

Those wishing to communicate to the Society should write to :

Honorary Secretary - ISCB
Dr. J. Seldrup
Ciba - Geigy Pharmaceuticals
Wimblehurst Road
Horsham
West Sussex
RH12 4AB U.K.

DISCLAIMER

The views expressed in this newsletter are not necessarily those of the ISCB and are entirely those of the contributors. The ISCB disclaims any responsibility arising from matters herein.

PROBLEMS AND OPINIONS

Some Epidemiological/Statistical Problems in The United Kingdom - A Personal View

There are numerous problems facing epidemiologists and statisticians today. One of the most important, complex, and pressing of these, both within the United Kingdom and elsewhere, is the Acquired Immunodeficiency Syndrome (AIDS) epidemic. Much has been learned about the epidemiology and pathogenesis of AIDS since the syndrome was first recognised in 1981. The aetiologic agent, Human Immunodeficiency Virus (HIV), and the main ways in which it is transmitted have been identified. However, a great deal of uncertainty remains about the future course and scope of the epidemic. For instance, how often, especially in 'after dinner' conversations, have you heard individuals predicting (usually based on little information) either that AIDS will have only a limited effect or that mankind will have died out by the early part of the next century!

Mathematical modelling of the epidemic has an important part to play in our understanding of and dealing with AIDS. Projections of future health care requirements are crucial for developing a coordinated approach for coping with the epidemic. The evaluation of the potential impact of intervention strategies intended to reduce the spread of HIV infection are essential in designing suitable public health policies. Statistical models may provide a better understanding of the key factors which allow or stimulate the spread of the virus, and they can also provide quantitative projections of the course of the epidemic under different conditions. In addition, statistical methods have both a role in quantifying the uncertainty associated with predictions of the numbers of HIV-infected individuals and AIDS cases and in estimating important factors such as the probability of transmission of the virus and the incubation period distribution.

There are, however, a number of features of the AIDS epidemic which complicate the development of statistical models. First and perhaps foremost, we still have relatively little information of an unbiased nature about the incidence and prevalence of the disease in the general population. Anonymous randomised testing, e.g. of pregnant women, has been advocated, especially within the epidemiological profession. However, support for such schemes is polarised not only among

the medical and nursing professions but also among politicians and the public. Secondly, although it is known that the principal methods of transmission of HIV are sexual intercourse and the sharing of contaminated needles among drug users, relatively little is known about the groups at highest risk of infection, including such basic information as the numbers of individuals involved. Furthermore, relatively little is known about their sexual and drug use behaviours, and the situation is further complicated by the changes in their behaviour due to increased awareness of AIDS. It is extremely difficult, if not impossible, to develop strategies to alter risky behaviour if one does not know what is presently occurring. Thirdly, much remains to be learned about the epidemiology of HIV and its transmission, and also the natural history of HIV infection and its development into AIDS. For instance, how infectious is an HIV-infected person and does his/her infectiousness change over time? Is the transmission from male to female more likely than from female to male and under what conditions? Also, the long-term effects of HIV infection in an individual are unknown.

Although research into HIV and AIDS is vital, it is important that the funding of such work is carefully organised so that efforts are not duplicated (in the same way that cancer research is coordinated in this country) and trivial work is not funded at the expense of significant fundamental research. Judging from the number of academic departments carrying out AIDS-related research and the number of applications for grants to do such work, one might cynically conclude that it is essential to get on the AIDS 'bandwagon' because in times of financial stringency in academia, such work offers the opportunity for extra, much-needed funding.

Heart disease and cancer continue to occupy the attention of many epidemiologists in this country. In the present century, two of the major 'epidemics' in Western society have been in coronary artery disease and lung cancer. The mortality rate from coronary artery disease is declining in the USA, Australia and New Zealand much faster than in the UK, although the reasons are unclear. The mortality rate from lung cancer is also declining in men, due primarily to the decrease in cigarette smoking, but the same does not appear to be occurring among women. The 'epidemic' is less mature in women and, therefore, we will not see the same decline among women for some years to come. Indeed, if current trends persist, lung cancer will replace breast cancer in women in

England and Wales; it has already done so in Scotland. Unfortunately, in spite of the immense epidemiological effort focused on cancer, major improvements in terms of a significant decrease in the incidence and mortality have not generally occurred. The death rate from stomach cancer is declining in this country but not as a result of any epidemiological effort (nor any treatment effect)!

Genetic research appears to offer hope of advancement in some areas of cancer research. The importance of identifying the defective genes which cause diseases such as Huntington's chorea or cystic fibrosis, so that ante-natal diagnosis may be made and genetic counselling given, is obvious. Some of the more common cancers also seem to have a genetic component in some situations, as well as an environmental one. In families with a number of cases of a particular cancer (especially one which develops later in life), the identification of the abnormal gene(s) may lead to the detection of other family members who are at risk; these individuals could then be offered regular screening or even prophylactic treatment. In the future, the identification of abnormal genes in cancer patients could not only lead to a greater understanding of the role that genes play in the development of cancer and, hence, a greater understanding of the disease itself, but also may open up the possibility of genetic therapy.

One of the topical and controversial questions in cancer epidemiology is whether the clusters of childhood leukaemia cases occurring in the vicinity of Dounreay, Sellafield and other nuclear establishments are directly related to the activities of these plants and, if so, what the causal explanation is. The increased risk of childhood leukaemia is not high but is clearly of concern. It is possible that the aetiological agent is a virus, but it is hard to suggest what the virus might be and how it might be transmitted. Unfortunately, the subject tends to raise deep personal feelings and many seem unable to view the evidence objectively which leads to heated debates, often influenced more by beliefs and prejudices than facts.

Yet another controversy, which has rumbled on for many years, is whether oral contraceptives (OCs) can cause breast cancer. During the 1970s, over 20 epidemiological studies were performed in which the relationship between OCs and breast cancer was investigated. These studies were generally reassuring with no overall increase in the risk of breast cancer among OC users when compared with 'never users'.

Nevertheless, anxiety concerning a possible risk was not completely allayed for two important reasons. Firstly, it is possible that there is a long latent period between exposure and the clinical appearance of cancer and the early studies could not have detected such an effect. Secondly, although 'ever use' of OCs was generally found to be unassociated with an increased risk of breast cancer, two studies reported significantly increased relative risks among women who had used OCs before their first full-term pregnancy and, in one of these two studies, a highly significant trend of increasing risk with duration of use was found in these young women. These latter results caused widespread concern because there are biological reasons why the risk of developing hormonally-induced cancer might be greater among such women.

At the beginning of the 1980s, the question concerning the possible association between OCs and breast cancer remained unresolved. While there was no evidence of increased risk among older parous users, longer follow-up of exposed cohorts and new case-control studies of women who had been exposed as long as 20 years before diagnosis were required. Also, further studies of women who had taken OCs for long periods at an early age and before their first pregnancy were needed. Results from three cohort and nine major case-control studies have been reported subsequently and all have failed to detect any risk among older parous women. However, the results for women with a long duration of use at young ages or before first full-term pregnancy are conflicting, and the question remains unanswered for these women. In these sub-groups, either a significantly increased risk with evidence of a dose-response relationship, was found or no association, i.e. a relative risk of around unity, was observed; no study detected a significant protective effect of OC use. It is possible that the negative studies may have failed to find an association because of the effects of latency or because they did not include sufficient numbers of women with long durations of use. On the other hand, it is possible that the increased risks found in the other studies could have been due to bias or even chance, although the latter seems unlikely. The slight trend towards positivity in the studies tends, however, to support the view that, in these sub-groups of young women, OC use is associated with an increased risk of breast cancer. Further follow-up of one of the cohort studies and the results of another large case-control study are due soon; it will be most interesting to see in which direction they point.

The OCs and breast cancer debate and other similar problematic areas raise another important epidemiological / statistical question, which is how does one assess relative risks of, say 1.4 - 1.8, especially in uncontrolled studies? The importance one should place on such results is often unclear. For example, a recent epidemiological study showed that the risk of Alzheimer's disease in people under the age of 70 years, calculated using rates estimated from the records of CT scanning units in 88 county districts of England and Wales, was 1.5 times higher in districts where the mean aluminium concentration exceeded 0.11 mg/l than in districts where concentrations were less than 0.01 mg/l. The authors of the study concluded that their results provided evidence of a causal relation between aluminium and Alzheimer's disease but did not rule out the possibility that the observed association was due to an unknown confounding variable. The assessment of the possibility of causality is traditionally based on criteria such as: Is the relative risk large? Have similar findings been obtained elsewhere? Is there a dose-response relationship? Do animal experiments and laboratory studies support the association? Is the association consistent with known facts about the disease? The authors of the Alzheimer's disease study did not answer these questions. This is not surprising because it is often difficult to answer them. Nevertheless, how does one judge such results?

Whether or not OC use leads to breast cancer is not solely a problem facing cancer epidemiologists; it is also of concern to pharmaco-epidemiologists. Pharmaco-epidemiology is a small but important (and growing) area of epidemiology. Those working in it are concerned with the early detection of adverse reactions to drugs. Public attention has not been focused on their work recently because, fortunately, there have been no major drug problems that have attracted the attention of the media. In the United Kingdom, efforts in post-marketing surveillance (PMS) are fragmented and are likely to continue to be so. We have two national PMS systems, i.e. the Committee on Safety of Medicine's voluntary reporting scheme (the 'yellow card scheme') and Prescription-Event Monitoring run by the Drug Safety Research Unit in Southampton; both have their disadvantages. Elsewhere, there are commercial schemes organised by market research companies who supply free computers to general practitioners so that they can computerise their practice records (allegedly an advantageous thing to do). In

return, the GPs agree to let the companies take anonymous details from their case notes for market research into drug use and also the possible detection of adverse drug reactions. So far, nothing of any value seems to have been achieved by these commercial schemes. There are also a few local schemes, usually centred around hospitals, and a small scale record linkage scheme in Tayside, Scotland, which has been investigated for its potential PMS use. Finally, pharmaceutical companies are performing more post-marketing research. Much of it is post-marketing clinical trials. Few pharmaceutical statisticians have expertise in pharmaco-epidemiology. Nevertheless, some useful PMS has been carried out within the industry. In my opinion, however, it is unlikely that important questions, such as 'do non-steroidal anti-inflammatory drugs cause peptic ulceration?', will be answered in the near future with the present methods (some, of course, believe that a causal relationship has been 'proved', but the evidence is poor). Only if computerised medical record linkage on a large scale is established in this country will there be a chance of solving this and other complex pharmaco-epidemiological problems.

This brief essay on some of the difficulties facing epidemiologists and statisticians in the United Kingdom today represents my interests and those of some of my colleagues. It is not intended to be comprehensive. I hope that my contribution to 'ISCB News' will stimulate other members to write about their problems and interests.

Nigel Lawson
Block D, 15 Cotswold Road,
The Institute of Cancer Research,
Belmont, Surrey SM2 5NG.

ISCB - Membership

Those interested in joining the Society should write to the Hon. Treasurer, Dr. Douglas W. Wilson, Tenovus Institute for Cancer Research, Heath Park, Cardiff CF4 4XX, U.K.

Fees for 1989: Ordinary Membership £15; U.K. Subscribers to 'Statistics in Medicine' (plus membership) is £90, Non-U.K. subscribers (plus membership) is £100. All cheques, made payable to ISCB, and to be drawn on a British bank, or paid by other means so as to avoid bank charges.

DIARY OF EVENTS

Event	Date	Place	Contact
International Society for Chronobiology, (Time Series in Biology)	20-24 June 1989	Washington, USA	Dr.D.K. Hayes, USDA, ARS, NER, AEQI, Livestock Insect Laboratory, RM 120, Bldg 307, BARC-E, Beltsville, Maryland, MD 20705, USA
European Society for Chronobiology (Time Series in Biology)	15-18 July 1989	Cracow, Poland	Jozef Surowiak, Jagiellonian University, Institute of Zoology, Dept of Animal Physiology, 30-060 Krakow, ul M Karasia 6, Poland Tel : 34 - 00 - 25
Nordic Regional Meeting of the Biometric Society	21-23 Aug 1989	Laugarvatn, Iceland	Holmgeir Bjornsson, Agricultural Research Institute, Keldnaholti, 112 Reykjavik, Iceland
International Conference : Health of Inner Cities and Urban Areas	4 - 7 Sept 1989	Cardiff, Wales	Mrs L Butterworth, Meeting Point West, Paramount House, 77 Mutley Plain Lane, Plymouth PL4 7DS Tel: 0752 225512
Statistical Methods in Biopharmacy	7-8 Sept 1989	Paris, France	Joris Cauquil, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France
Errors, Uncertainties and Bias in Astronomy	11-14 Sept 1989	Strasbourg, France	Professor C Jaschek, CDS - Observatoire Astronomique, 11 rue de l'Université, F-67000 Strasbourg
IUSSP XX1st General Population Conference	20-27 Sept 1989	New Delhi, India	Bruno Remiche, IUSSP, 34 rue des Augustins, B-4000 Liege, Belgium
Robustness in Statistics	2 - 7 Oct 1989	F R Germany	J Konig, ECAS 89, Institut fur Med. Biometrie u. Med. Inf., Universitat Heidelberg, Im Neuenheimer Feld 325, D-6900 Heidelberg 1, F R Germany Tel:06221 5642156

Book Review

Numerical solution of ordinary differential equations - for scientists and engineers.

by L.Fox and D.F. Mayers

Chapman and Hall, London and New York (1987). 249 pp.

This book discusses the numerical solution of ordinary differential equations in ten clear, readable chapters. As the title suggests, the book is intended for readers from a science or engineering background, but some knowledge of mathematics is assumed. Anyone who has studied mathematics as a subsidiary subject at university level should have no difficulty in understanding the book. Chapter 1 is an introduction to the subject and its terminology, citing some simple examples to aid explanation. The subject of Chapter 2 is sensitivity analysis which is of particular relevance to practical scientists and engineers concerned with errors of measurement. The solution of both initial-value and boundary-value problems is covered comprehensively in Chapters 3 to 7 paying attention to the economical use of computation time and memory. In Chapter 8 advice is given on the use of some of the algorithms currently available from software libraries, and in Chapter 9 there is a bibliography with brief comparisons of some of the methods contained in the references.

Throughout the book there are many worked examples and exercises for the reader with answers provided in Chapter 10, but it is a pity that almost all the examples given are expressed in pure-mathematical terms. The book would be far more attractive to its intended readership if more reference were made to familiar problems in science and engineering. Nevertheless, this book should prove a useful addition to science and engineering libraries.

H Griffiths, 17 January, 1989.

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