MATHEMATISCHES FORSCHUNGSINSTITUT OBERWOLFACH

T a g u n g s b e r i c h t 7/1983

Medizinische Statistik

6.2. bis 12.2.1983

Bei dieser von den Herren P. Ihm (Marburg) und H. Klinger (Düsseldorf) geleiteten Tagung über medizinische Statistik bildete der Themenbereich "statistische Entscheidungen" einen Schwerpunkt. Durch Vorträge zu aktuellen Einzelfragen wurde die Tagung abgerundet. Die Themen wurden sowohl aus theoretischer Sicht wie auch unter Berücksichtigung der in der Praxis gegebenen Bedingungen behandelt. Die anschließenden Diskussionen ergaben einen - oft bis in die Nachtstunden fortgesetzten - fruchtbaren Gedankenaustausch zwischen den mehr theoretisch orientierten und den der Praxis nahestehenden Teilnehmern, bei dem die Problematik der Umsetzung theoretischer Konzepte in die tägliche Routine und die Schwierigkeiten bei der Konstruktion adäquater Modelle für spezielle Fragestellungen immer wieder im Mittelpunkt standen.

Vortragsauszüge

K. ABT:

Criteria for the Efficacy of Diagnostic Tests and the Theorem of Bayes

With $S_e = P(\oplus \mid K)$:= Sensitivity of a diagnostic test := probability of positive test result given disease K, and with $S_p = P(\ominus \mid \bar{K})$:= Specificity := probability of negative result given non-K, according to Feinstein (Clin. Pharm.and Ther.1975) high S_e is desired for a discovery test and high S_p for a confirmation test; but these qualities are not sufficient for a high efficacy of a test in the application phase. Therefore, the "predicted values" $PV_p = P(K \mid \oplus)$ and $PV_n = P(\bar{K} \mid \ominus)$, respectively, have been proposed as criteria for the evaluation of competing tests (Galen and Gambino, Wiley 1975). It is shown that PV_p and PV_n are very insensitive to S_e and S_p, respectively, for small values of $P_r = P(K)$:= prevalence of K in population considered, and the criteria $I_{S_e} = PV_p \times S_e$ and $I_{S_p} = PV_n \times S_p$, respectively, are proposed instead. Since particularly PV_p is highly dependent upon - and monotonically increasing with - P_r, the population sampled in the test evaluation phase should be the "suspected" population, i.e., the same as the one a patient is drawn from in the application phase, whereby the prevalence P_r of K in the population under consideration is increased. The same argumentation is used with respect to Bayesian diagnosis, where a positive test result corresponds to a symptom present and where the set of competing diseases K_i should include only diseases presumably present in the suspected patient population.

A.C. ATKINSON:

Optimum Biased Coin Designs for Sequential Clinical Trials with Prognostic Factors

Patients in a clinical trial arrive sequentially and are to be assigned to one of t treatments. This assignment should maintain a balance between the numbers receiving each treatment, yet should be sufficiently random to avoid any suspicion of conscious or unconscious cheating. The theory of the optimum design of experiments is used to provide designs of the biased coin type for sequential clinical trials in the presence, or absence, of prognostic factors. The designs avoid many of the arbitrary features of earlier schemes.
Some mention is made of problems arising in the analysis of experiments such as these which are generated by restricted randomization.

R. AZENCOTT:

Some Remarks on ARMA Models Estimation

Consider a stationary process X verifying
$\sum_{k=0}^{p} a_k X_{n-k} = \sum_{l=0}^{q} b_l W_{n-l}$ where W is the innovation of X.

In estimating (a) and (b), the preliminary stage of computation which writes the systems of equations linking (a) and (b) to the covariances of X involves one tricky point: the system giving (b) has a finite number of solution and cannot be solved explicitly. We propose improvements over the well worn Box Jenkins approach - Namely:
1) how to compute all solutions quickly, from a given one
2) how to choose the right solution, 3) a direct computation of the (b) not involving iteration but rather series expansion which are very easy to compute.

J.A. BATHER:

Towards a more Rational Allocation of Treatments in Medical Trials

Three allocation rules are compared by assessing their effectiveness in discovering which of two treatments has the higher probability of success. The number of observations needed to obtain a given level of precision can be minimised by using a fixed-sample rule, but this involves too many applications of the inferior treatment. It is demonstrated that sequential allocation rules can achieve a similar pattern of error probabilities for a small fraction of the expected cost to the volunteers employed in the experiment.

P. BAUER:

Sequentially Rejective Two-sided Test Procedures

For the two-sided multiple test situation, a sequentially rejective test procedure is suggested. It is shown to have the multiple significance level α and to be less conservative than HOLM's (1979) procedure, which is applicable to the two-sided case if the set of k-two-sided hypotheses is replaced by a set of 2k one-sided hypotheses.

M. BRESLOW:

Methods of Analysis of Epidemiologic Cohort Studies

Grouped cohort data are considered consisting of numbers of cause-specific deaths D_{jk} and person-years denominators T_{jk} classified into J (age, sex, calendar year) and K exposure categories. A Poisson model $D_{jk} \sim P(\lambda_{jk} T_{jk})$ is

assumed with three possible structures for the death rates:

$$(I) \quad \lambda_{jk} = \lambda_j \exp(\beta z_{jk})$$

$$(II) \quad \lambda_{jk} = \lambda_j (1 + \beta z_{jk})$$

$$(III) \quad \lambda_{jk} = \lambda_j + \beta z_{jk}$$

Here the λ_j are nuisance parameters, z_{jk} a vector of covariables describing the effects of the exposures and their interactions with stratum variables, and β a vector of regression coefficients. An analogous series of models with the λ_j proportional to known standard rates is also considered. Problems of Maximum Likelihood estimation under model II are demonstrated. Knowledge of the external rates contributes more to β estimation in model III than in model I .

E. BRUNNER:

Rangtests in 2 x 2 Plänen

In der Literatur finden sich viele Ansätze zur Auswertung mehrfaktorieller Versuchsanlagen mit Rang-Tests. Möglichkeiten und Grenzen solcher Auswertungsmethoden werden gezeigt. Für das 2-Faktor-Modell werden Funktionale von Verteilungsfunktionen definiert, deren Beziehung zu den bekannten Parametern α, β, γ (Haupteffekte und Wechselwirkung) unter H_o und H_1 untersucht werden. Es wird gezeigt, daß unter H_o alle Funktionale frei von Störparametern sind, unter H_1 jedoch von je 2 oder sogar allen anderen Parametern abhängen. Die angegebenen Funktionale werden über empirische Funktionale konsistent geschätzt; dabei erhält man "auf natürlichem Wege" Rangzahlen; über eine Erweiterung des Satzes von Chernoff und Savage wird die asymptotische Verteilung der Schätzer bestimmt. Die asymptotische Varianz ist verteilungsabhängig; sie kann durch spezielle Ränge konsistent geschätzt werden, so daß man asymptotisch verteilungsfreie Tests erhält. Die Statistiken für den vollständigen

Zufallsplan, den Split-plot Plan und 2-Faktor Blockplan unterscheiden sich nur durch eine andere Varianz. Anhand von Gegenbeispielen wird gezeigt, daß eine Erweiterung auf mehr als je 2 Stufen je Faktor (wie sie z.B. von Conover und Iman, Lemmer und Stoker angegeben sind) zu unsinnigen Testverfahren führt.

U. FELDMANN:

Prediction of Multiple Identification Numbers

For patient identification as well as for optimized base access algorithms in computer aided hospital information systems identification numbers are used.
A 9 digit identification number, in Germany called "I-Zahl", consists of the following patient data:
Birthday (DD), Birthmonth (MM), Birthyear (JJ), a name-key (NN) and the sex (S). A tenth digit (Q) is used as a counter for multiple occupied identification numbers.
In order to estimate observed multiple occupied identification numbers, the usual binomial distribution approach fails. A Markov chain approach is offered, which takes observed frequency distributions of the several components of the identification number into account, and leads to good correspondence between observed and estimated multiple occupied identification numbers. Nearly 150 thousand different patients from the Medical School of Hannover were analyzed. This approach is used for further prediction.

U. FERNER:

Charakterisierung von "Norm"-verläufen zur Diagnoseunterstützung

Bei depressiven Patienten sind häufig vegetative Funktionen gestört, die sich mit dem Abklingen der Krankheit normalisieren und somit ein objektives Maß für Tiefe und Verlauf des Geschehens darstellen können (KIELHOLZ,1982). Als besonders empfindliche Kreislaufreaktion kann die Messung der Durchblutung der Finger anhand der Wiedererwärmung der Fingerspitzen nach einer kurzen Abkühlung betrachtet werden. Durchschnittliche Verläufe dieser Reaktion und deren Variabilität beim Gesunden sind Voraussetzung für eine Bewertung der beim depressiven Patienten erhobenen Werte.
Diese sog. "Norm"-Werte wurden an einer Stichprobe ($n = 285$), die bzgl. Geschlecht und Altersklassen ausbalanciert wurde, erhoben. Die individuellen Verläufe werden durch 9 Meßpunkte (vor und nach Abkühlung, sowie während 2,4,6,8,10,15 und 20 Min. in der Wiedererwärmungsphase) beschrieben.
Es läßt sich zeigen, daß die - unvermutet - heterogenen Verläufe durch 3 ausgewählte Parameter sich in 4 homogene Klassen verschiedener Reaktionstypen einteilen lassen. Das dabei angewandte methodische Vorgehen wird schrittweise vorgestellt und die erhaltenen Ergebnisse vor allem bzgl. ihrer Aussagekraft diskutiert.

G. GIANI:

A Generalized Selection Problem with Special Attention to Binomial Distributions

Considering only two populations the relation of the selection problem in the classical indifference zone formulation to the Neyman-Pearson test theory is demonstrated via two examples.

For distribution functions with location parameter and binomial distributions it is shown that the problem of selecting the best population can be solved by a one sided test problem with $\alpha = 0.5$. Afterwards a generalized selection problem is formulated. The goal is to select s populations which contain at least r of the t best ones. For binomial distributions the problem is solved to control the probability of correct selection over the preference zone at any preassigned level. New confidence statements are given in this context.

SH.M. GORE:

The Curability of Breast Cancer

Three methods of comparing observed and expected mortality - the age corrected lifetable, ratio of observed to expected deaths and excess death rate - are discussed. The excess death rate is found to be the most satisfactory measure and for five year survivors in the Western General breast cancer series is shown to decrease exponentially. An additive hazard model is proposed in which the hazard in the cancer series is the sum of an underlying hazard estimated from Scottish national data and an excess hazard which is a function of covariates which decays exponentially at a rate which may also depend upon covariates.

R. HILGERS:

Remarks on Random Effects

It is demonstrated how even small random (block-/interaction-) effects may influence group-sequential decisions. The argumentation may be extended to long-term and multi-centre studies as well as to the comparison of independent studies.

G. HOMMEL:

Multiple Test Procedures for Arbitrary Dependence Structures

If for a multiple testing problem the structure of hypotheses is known, one obtains a multiple test procedure (MTP) which keeps a multiple level α when the following conditions hold: (i) the system of hypotheses is $\cap$-closed; (ii) the MTP is coherent; (iii) each single test keeps the "local" level α. If the structure of hypotheses is not taken into account, one can use the power set of $\{1,\ldots,n\}$ as an index set for the system. Though such a MTP need not be coherent, one can ensure by a slight modification of conditions (i) and (ii) that it still keeps the multiple level α.
This principle can be applied to the Bonferroni and to HOLM's (1979) procedure. Moreover, one obtains several simultaneous and sequentially rejective MTP's by using the inequality of RÜGER (1978) or related methods.

P. IHM:

Das Vaterschaftsproblem im Lichte der Entscheidungstheorie

Bei strittiger Vaterschaft eines unehelichen Kindes wird im allgemeinen eine Blutgruppenuntersuchung durchgeführt. Dabei betrachtet man die Wahrscheinlichkeiten der Phänotypkombination beim Tripel Kind-Mutter-Vater, die unter den Hypothesen H_o (Vaterschaft) und H_1 (Nichtvaterschaft) kurz X bzw. Y bezeichnet werden. Entschieden wird auf Grund des Likelihood-Verhältnisses $\lambda = Y/X$ $(X \neq 0)$. Seien α und β die Fehlerwahrscheinlichkeiten erster und zweiter Art, A und B die mit den Fehlentscheidungen verbundenen Kosten. Entschieden wird bei $\lambda < \lambda_o$ für H_o, bei $\lambda \geq \lambda_o$ für H_1. Nach dem Minimaxprinzip ist λ_o Lösung von $B\beta/A\alpha = 1$, nach dem Bayesprinzip von $BqY/ApX = 1$, d.h. $\lambda_o = Ap/Bq$; p ist die a-priori-Wahrscheinlichkeit der Vaterschaft, $q = 1 - p$. Beim Einmannfall ist $p \approx 0.85$, wie aus größeren Stichproben ermittelt werden konnte. Aus dem Verhalten der deutschen Richter folgt $B/A \approx 550$.

H. IMMICH:

Decisions Taken by Large Surveys

Decisions which are not based upon controlled conditions like randomization or comparison groups are very frequent in medicine. A survey on aorta-to-coronary artery bypass surgery is considered as an example. 1096 consecutively from January 1974 till April 1978 collected patients which received bypass grafts were followed-up quarterly till January 1979. The aim of this survey was to analyze a number of intraoperative factors in terms of their effect upon survival and symptomatic improvement. After yielding remarkable results the authors decide to applicate in future at least as many grafts as vessels diseased and, if necessary, one graft more. A more accurate analysis of the data shows that the authors have taken their decision before starting the survey, only based on increasing skilfulness and practice. However, the decision was right.

R. JIROUŠEK:

Sequential Decision-Making Methods

There is a lot of decision-making methods and models used for computer-aided decision in medicine and they can be classified according to many different criteria. In my contribution I would like to present reasons emphasizing the importance of sequential methods and to show that there are situations that cannot be succesfully treated but using sequential methods. Three statistical decision-making methods and areas of their applications will be illustrated with medical examples. In addition to the classical Wald's Sequential Test, the Strategic Test and the Sequential Questionnaire will be presented.

W. KÖPCKE:

Repeated Significance Tests and Multiple Comparisons in Clinical Trials

Interim analyses are often performed in clinical trials. One reason for such analyses is the early stopping of the trial, if the treatment differences are convincing. The statistical method, which is often used in such situations, is the group-sequential approach (Pocock, 1977, O'Brien-Fleming, 1979, Köpcke, 1982). Since the group-sequential design is limited to one response variable and in many clinical trial we have more than one response variable, it is proposed to use the group-sequential design together with the Bonferroni-Holm multiple test procedure. Simulation studies using the data of the Timolol-study (N Eng Y Med 1981) indicate that it is unrealistic to have more than 5 interim analyses and more than 3 response variables.

ST.L. LAURITZEN:

Interaction Models for Mixed Data

We discuss an attempt to define a class of models suitable for the description of interactions among data, that are partly of qualitative and partly of quantitative type. The models are generalisations of log-linear models for contigency tables and covariance selection models.

V. MAMMITZSCH:

An Axiomate Approach to Least Square Theory

Three axioms are formulated which in the case of normally distributed observations lead to the well-known least square estimator. It is discussed how these axioms have to be changed in order to apply to the case of non-normal observations, too. Finally, random observations are considered which have their values in a separable Hilbert space.

D. MACHIN:

Models for Selecting Medical Treatments

Colton (1963) introduced a decision theoretic model for clinical trials. In the context of a clinical trial for comparison of two treatments, A and B, his fixed-sample-size design consists of the selection of 2n patients with a disease, n of which are randomised to receive treatment A the remainder treatment B. At the end of the trial a decision is taken to use one of the two treatments on future patients with the disease. The design problem is to determine the optional value of n.
To solve this problem Colton (1963) assumes a fixed number N of patients with the disease (the patient horizon). Outcome of treatment is normally distributed with unknown mean but known variance. The only cost involved is an ethical cost which is proportional to the true difference between treatments δ and δ has a normal prior with mean zero and variance σ_o^2.
Several workers have modified the basic Colton model but the model remains untested clinically.
The purpose of this paper is to review and suggest some modifications to the model and to indicate why such models are unlikely to be adopted (for serious diseases at least) in the near future.

J. MAU:

On Risk Extrapolation for Carcinogens Using Animal Data

The combination of two classifications of dose-response models allows to predict the ranking of added tumor risk at small dose levels taken from different models. Several types of construction of such models are considered when only a time-inhomogeneous Poisson process with dose-dependent cumulative

hazard function is assumed. In particular, a proportional hazards regression model of the form $(\lambda x + \lambda_o)^{\vartheta} \Lambda_o(t)$ may be used, with $x \geq 0$ denoting the dose level, Λ_o a cumulative baseline hazard function of time and $\lambda_o \geq 0$, $\lambda, \vartheta \geq 0$. If a multi-event type of construction as applied to "independent" or to "additive" action models, then a time-dependent generalized gamma model or a time-dependent multi-stage model (ϑ positive integer) may be obtained, respectively. Special cases of the former are time-dependent versions of the commonly used multi-hit, Weibull and probit models.

H. NOWAK:

How Useful are Statistical Decisions for the Management ?

The motivation for installing biometrical departments e.g. at pharmaceutical companies, may be classified into three groups: rationalizing, objectivity, function of alibi. Regarding the first two points it is shown by examples that quite often biometrics does not give the help wanted in making decisions in management, and thus management feels left alone. The main question is how to combine the results within one clinical trial and how to combine all trials into one global decisions on the drug. A heuristic approach herefore is outlined.

R. REPGES:

Identifiability of Parameters

Starting with a concrete biological question, a model $M(\vartheta)$ is formulated, $\vartheta \in \Theta$, together with the experimental observation $y(\vartheta)$. Within a linear frame work it is possible to determine the set $H \subset \Theta$ such that for all $\vartheta \in H_y$ we have the same observation $y(\vartheta)$. In the special situation it turned out that H contains only one element - ϑ is globally identifiable. Usually H consists of a second degree subspace or contains at most countably many points of Θ.

P. ROEBRUCK:

A Posteriori Decisions

The demand for the valuation of effects detected by looking at the data, arises from many practical situations, particularly in clinical trials. In general, Neyman-Pearson-tests should not be applicated for a posteriori hypotheses. Assuming that nullhypotheses, which are not tested are retained, provides an adequate model for what happens, if such tests are actually carried out. It results, that given only one latent testing problem the first kind error probability is kept as if the testproblem would have been given apriori. For more then one testingproblem, however, the multiple first kind error probability may be very great if it is permitted to select a subset of them for testing. This is true particularly, if selection is made in order to get as many rejections as possible. Therefore it seems to be not justifiable to give explorative p-values to physicians not being familiar with such problems, because p-values mostly are interpreted in the sense of Neyman-Pearson tests.
As an alternative approach it is proposed to use aposteriori probabilities of the respective nullhypotheses, given a suitable prior, which quite general may be interpreted by physicians in an intuitive manner and without the danger of being confused with Neyman-Pearson-tests.

S. SCHACH:

The Estimation of the Regression Parameter in Cox' Proportional Hazard Model - Report on a Simulation Study

In the analysis of survival times one often uses the Cox model which assumes that the hazard of failing at time t is given by $\frac{f(t)}{F(t)} e^{z'\beta}$, where $f(\cdot)$ and $F(\cdot)$ are the density and survivor function of a base survival time and z is the vector of covariates. β is the parameter of interest. It is estimated by maximising the "marginal likelihood".

It is shown, that with 64 observations and 5 paramters the maximum likelihood estimator is on the average about 10% too large, as compared to the true values. This fact persists in the case of censoring, however in the presence of ties it gets reversed. Recommendations for methods of removing the bias were discussed.

J.R. SCHÄFER:

Comparison of Different Discriminant Procedures with Data of Mixed Scale-Type, used in a Triage Decision Problem for Patients with Chest Pain

Overadmission to the coronary care unit (CCU) is a well known problem in cardiology. To increase the accuracy of the triagedecision for patients with chest pain, the use of discriminant analysis may be helpful as a decision aid for the physician on duty. For about 2000 patients validated data of mixed scale-type and unknown distribution have been collected. The problem is to find the best discriminant procedure for this set of data. Out of the large list of published discriminant procedures three (linear discriminant analysis, kernel estimates with mixed kernels, Lancaster-model of second order) are selected for comparisons using binary, ordinal, metric and mixed data. The goal of these comparisons is to estimate differences in discrimination power for these procedures using various types of data. By that way a method may be derived to estimate influences of reasons for "losses in classification accuracy" using a non-optimal discriminant analysis.

M. SCHUMACHER:

Analysis of Multiple Endpoints in Clinical Trials

In clinical trials, in particular in cancer clinical trials, one often is interested to assess the effects of a treatment with respect to a general criterion, the survival time, as well as to more specific criteria, disease recurrence for example. Current methods based on so-called disease-free survival are criticised on the grounds that they confuse events, such as disease recurrence and death and consequently could be very misleading. Alternative methods of analysis based on separating the measures of treatment effect using "event-specific" hazard and cumulative hazard functions are presented. The methods proposed are illustrated by using data on stage I breast cancer patients from the Manchester Regional Breast Study.

E. SONNEMANN:

Multiple Tests of Paired One-Sided Hypotheses

Let X be a random variable with distribution $P_\vartheta, \vartheta \in \Theta$. If one tests n real parameters $\mu_i = \mu_i(\vartheta)$ two-sided, i.e. $H_{oi}^{=} : \mu_i = 0$, then in case of rejection one wants to know whether $\mu_i < 0$ or $\mu_i > 0$ can be assumed. Thus the problem consists in testing n pairs of one-sided hypotheses, $H_{oi}^{\leq} : \mu_i \leq 0$, $H_{oi}^{\geq} : \mu_i \geq 0$. The sequentially rejective HOLM-test (1977/79) provides a solution with critical levels $\alpha_i = \alpha/(2n+1-i)$, where α denotes the multiple level to be kept. These levels are slightly improved by

$$\tilde{\alpha}_1 = \frac{\alpha}{2n}, \quad \tilde{\alpha}_{r+1} = \frac{\alpha - \tilde{\alpha}_r}{2(n-r)}, \quad 1 \leq r \leq n-1$$

If one removes the non-continuity out of the problem and tests the $2n$ null hypotheses $H_{oi}^{\leq} : \mu_i \leq 0$, $H_{oi}^{>} : \mu_i > 0$, one may choose all n critical levels equal to α/n.

D. SPIEGELHALTER:

Predictive Accuracy of Biopsy following Heart Transplantation

After a heart transplant the immuno-suppressive regime is primarily governed by the results of biopsies of the heart muscle. However, since cell damage is not uniform over the heart wall, the possibility of false-negative results has led to multiple specimens being taken at each session. The problem remains to estimate the predictive probability that no rejection is taking place after a series of negative specimens, bearing in mind that the true state is never known.
Formulation as a latent structure problem leads to the use of the EM algorithm to estimate the predictive accuracy of the procedure.

H.J. TRAMPISCH:

Adaptive Estimators for Cell Probabilities

For the m-dimensional contingency table with z cells let $N(a)$ be the absolute cell frequency in cell $a \in S$ $(|S| = z)$ in a sample of size n. The relative frequencies $M_n(a) = \frac{N(a)}{n}$, $a \in S$ are Maximum-Likelihood estimates of the cell probabilities $p(a)$. Let $U_n(a)$ be a further estimator of $p(a)$ $(U_n(a) \geq 0$, $a \in S$, $\sum_{a \in S} U_n(a) = 1)$. We consider the linearkombination $\tilde{p}_n(a,s_n) = (1-s_n)M_n(a) + s_n U_n(a)$. Now we are looking for an s_n^* such that with $p_n^*(a) = \tilde{p}_n(a,s_n^*)$ the mean squared error $MS = E \sum_{a \in S} (p_n^*(a) - p(a))^2 = \min_{s \in [0,1]} E \sum_{a \in S} (\tilde{p}_n(a,s) - p(a))^2$ is minimized. The optimal weighting factor s_n^* for sample size n for the estimator $U_n(a)$ for given $p = (p(a))_{a \in S}$ is given by

$$s_n^*(p) = \frac{\sum_{a \in S} \mathrm{Var}(M_n(a)) - \sum_{a \in S} \mathrm{Cov}(M_n(a), U_n(a))}{\sum_{a \in S} E(M_n(a) - U_n(a))^2}$$

An estimator of $s_n^*(p)$ may be obtained by substituting p by the Maximum-Likelihood estimates $M_n = (M_n(a))_{a \in S}$, so $\hat{S}_n = S_n^*(M_n)$. By use of four distributions derived from empirical data two adaptive estimators are compared with standard methods.

J. WAHRENDORF:

Bootstrapping Observationed Studies

The bootstrap method (Efron, 1979) estimates the sampling distribution of a random variable $R(X,F)$ which depends on observations X sampled from an unknown distribution F. This technique is applied to the statistical analysis of epidemiological studies where X are the data collected (generally, number of individuals in certain disease/exposure categories), F the underlying sampling frame and $R(X,F)$ a relevant measure of the disease process. Application to the Mantel-Haenszel estimator and the analysis of interaction effects are given.

E. WALTER:

Two Remarks about Simpson's Paradox

1. Assume that in a population the success rates of two treatments are p_1 and $p_1 + d_1$ and in another population p_2 and $p_2 + d_2$. It is possible that in the pooled population the first treatment has a greater success rate. For the occurence of this paradox conditions are given. Provided $p_2 - p_1 \geq 0$, a necessary condition is $p_2 - p_1 > d_1$.

2. Assume there is a two-dimensional normal distribution $N(0,0,1,1,p)$, define conditional populations by the areas $(x + y < -c)$ and $(x + y > c)$ and dichotomize both at $x = 0$ and $y = 0$, then certainly we get the paradox, when $c \geq 2\Phi^{-1}(0.75) = 1.349$.

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