

FUZZY APPROACH TO META-ANALYSIS

Bracarense Costa, Paulo Afonso
Department of Statistics – Federal University of Parana- Brazil
bracaren@est.ufpr.br

Bastos, Rogerio Cid
Department of Industrial Engineering – Federal University of Santa Catarina - Brazil
rogerio@sei.ufsc.br

Kandel, Abraham
Computer Science Department – University of South Florida - USA
kandel@csee.usf.edu

ABSTRACT

Meta-analysis is a statistical procedure to do syntheses of evidences. In the production of scientific knowledge, in spite of paradigmatic skips of quality, the rising of the accumulation of acquired knowledge (based in carried studies) is, in the general, the way as science moves forward to accomplish new discoveries and to confirm other already obtained.

The methods developed for the attainment of the meta-analysis, analysis of analyses previously accomplished, have been developed during this century. More recently, starting from works of the half of the 70th, there was a great impulse in the meta-analytical methods, for have been extended to a great variety of areas of the knowledge, notably in the Education, Psychology and Medicine. Substituting the revision of narrative literature for more scientific forms of synthesis with the use of statistical instrumental of significance.

There are a little number of works published in meta-analysis. The main area of application is in medical research, and with sporadic applications of intelligent techniques in that field, if any. A concise discussion was done by MANTON ET AL.(1994), and more as suggestion of possibility of the use of their GoM (Grade of Membership) technique than as a consistent development in the area. The main meta-analytic methods were presented in the Panel on Statistics Issues and Opportunities for Research in the Combination of Information supported by the National Research Council of USA directed by J.R.Gaver, whose results were published by the National Academic Press. (GAVER ET AL., 1992). One of the most important book in the field was written by HEDGES AND OLKIN (1985). This book deals with statistical methods for meta-analysis. In the last year, a link between meta-analysis and analysis of sensibility was done by PETIT (2000), but without utilization of intelligent techniques.

Following the strong trend of paradigmatic change in the treatment with the ignorance and the uncertainty, the present work proposes a methodology for the meta-analysis accomplishment, incorporating to the random component of the uncertainty, another component that search uncertainties whose nature is not random. It is considered, then, the vagueness, the imprecision and the ambiguity in the statistical modeling of the meta-analysis, through the incorporation of concepts of Fuzzy Set Theory.

Basically the probabilistic-fuzzy model for a random sample is the product of multinomial model with cells of probability given by

$$\Pr(Y_{ijl} = 1.0) = \sum_{k=1}^K g_{ik} \lambda_{kjl}$$

For each question or measure j for the individual i y_{ijl} is the response represented by a set of L_j binary random variables. Then y_{ijl} is the empirical realizations of the random variable Y_{ijl} . The variable g_{ik} is used to represent the grade of membership to the i -th individual for the k -th extreme profile in a fuzzy partition of the sample space. See WOODBURY (1974) for more details. λ_{kjl} is the probability of a response "1" for the j -th question by the individual with the k -th extreme profile.

The traditional meta-analysis, as much in its classic approach as bayesian, is carried through pooling the significance levels or of the so called "effect size", of the original studies that are considered as sample units. The effect size is a measure of difference between statistics obtained by different treatments, standardized, in general, by a joint variance. Its necessity elapses of the fact that studies with close purposes, supply different measures of effect, what would disable the construction of a common measure for the several studies.

Based on the Manton model (MANTON ET AL. 1994) for diagnoses in the medical research, this work considers a probabilistic-fuzzy model, which has as independent variables the significance level, the sample size and the effect size of each study. As response the "relevance" of each study is looked for, based on those information, through the calculation of the probability of a study to be "relevant" or not. The variable relevance has a very clear meaning in clinical research, as much in the diagnosis as prognostic study. It is by nature a variable with linguistic values, which translates the human reasoning in the decision making. The deal with that variable can only be given in terms of mathematical tools that can represent it. Fuzzy Set Theory supplies those tools.

The suggested model intends to calculate the probability of relevance of the studies that compose the meta-analysis. And from those values search a joint value of those probabilities, that summarizes the findings in the particular studies. The model is intermediate between the analysis of the individual of the regular medical procedure and the analysis of set of individuals of the statistical methods. It builds, finally, a bridge between the "unique" and the "typical".

These fuzzy sets are define as linguistic variables. Considering the discussions around the p-value - CASSELA ET AL. (1996), GIBBONS AND PRATT (1975), HUNG ET AL (1997), and SCHERVISH (1996) - one stabilishes three sets: Highly significant, Significant and Non-significant. In the same way, based on COHEN(1988) and ALGINA(1995) one can define the fuzzy sets for effect size: Effect size large, Effect size medium and Effect size small. The two sets, Big sample size and Short sample size, was defined based on COCHRAN (1983), GOODMAN (1989) And OAKES(1993).

These three fuzzy sets define eighteen extreme profiles. The probability of the elements (studies in meta-analysis) in each extreme profile were given in the figure below. The elicitation and assessment of these probability are given by the method of preferences, or subjective probabilities of DEGROOT (1970) modified.

Extreme Profile	Large Sample			Small Sample		
	High.sign	Sign.	No sign.	High. Sign.	Sign.	No sign.
Large ES	1 0.99	2 0.95	3 0.50	10 0.98	11 0.90	12 0.25
Medium ES	4 0.79	5 0.76	6 0.40	13 0.62	14 0.58	15 0.16
Small ES	7 0.50	8 0.48	9 0.25	16 0.25	17 0.23	18 0.06

Figure 1 Subjective Probabilities of a individual of extreme profile k be relevante

These values must be weighted by the grades of membership of the particular results of a research by the extreme profiles. The grades of membership were done by the fuzzy sets difined above. For instance, a study with $n = 600$ (simple size), $ES = 0.4$ (effect size) and $p\text{-value} = 0.04$ will be:

$$\begin{aligned}
 P(\text{relevance}) &= \sum g_{ik}\lambda_{kj}, k = 1, K \\
 &= (g_{i4}\lambda_{4rel.})(g_{i5}\lambda_{5rel.})(g_{i7}\lambda_{7rel.})(g_{i8}\lambda_{8rel.})(g_{i14}\lambda_{14rel.})(g_{i16}\lambda_{16rel.})(g_{i17}\lambda_{17rel.}) = \\
 &= (0.11 \times 0.79)(0.20 \times 0.76)(0.11 \times 0.50)(0.20 \times 0.48)(0.17 \times 0.58)(0.11 \times 0.25)(0.17 \times 0.23) = 0.56 \\
 P(\text{relevance}/ n=600, es=0.4, p\text{-value}=0.04) &= 0.56
 \end{aligned}$$

The conclusion of these simulation is that: although the study present $p\text{-value}$ equal to 4%, traditionally significant, the relevance of the study is 56% because the effect size is to small. If one thinks in a 80% of relevance as a good level, the conclusion is not definitive for the alternative hypothesis.

The independent variables are considered as fuzzy sets, whose degrees of membership weight the subjective probabilities of a given element to belong to the components of a fuzzy partition of the sample space. ROMER AND KANDEL (1995) defined fuzzy partitions of the sample space in the context of hypothesis testing, It works therefore with two different measures of believe: fuzzy degree of membership and subjective probability.

The result obtained for each study is given in terms of the degree of relevance, determined by the calculated probability. The composition of those probabilities of fuzzy events will supply the degree of joint relevance of all the studies.

Given the probabilities of relevance of each study, it is now necessary to agregate this measures (fuzzy numbers) in some way. Considering heterogeneity between studies, a fix effect model is not adequated. The random effect model of meta-analysis is used throughtout the calculation of a weighted average of the variable in question (the probability of relevance), considering the inverse of variance (measure of information) as the weights.

The model was applied to a classic data set for the meta-analysis accomplishment in clinical research. At the 70-th, six big multicentric random clinical trials about the efficiency of the aspirin in tratement of pos-myocardio infartion (IM) by all causes, werre conduct in Europe and in the United Stats.

The six trials in consideration are done by (i) Elwood et al. (1974) denominated UK-1; (ii) Elwood & Swetnan (1979), UK-2; (iii) the "German-Autrian Multicenter Study",

GAMS, Breddin et al.(1979); (iv) the "Coronary Drug Project Aspirin Study", CDPA (1976), (v) the "Persantine-Aspirin Reinfarction Study Research Group", PARIS (1980) and (vi) the "Aspirin Myocardial Infarction Study Research Group", AMIS (1980). All the trials were conducted during the period from 1970 to 1979. All of them were randomized, controlled by placebo, double-blind and multiclinics. A synthesis of each experimental design, can be found in CANNER(1983). A lot of meta-analysis was done, using several methods. This paper desires to discuss comparatively the results obtained by the fuzzy-probabilistic approach with the results obtained by these others methods. One intends to show that incorporating the medical expert opinion, through the determination of the fuzzy sets (independent variables) and the construction of the subjective probability, can improve the results. The main outcome obtained by these study is that the aspirin is not so efficient, as it is usually accepted.

REFERENCES:

- ALGINA, J., R.C. BLAIR and W.T. COOMBS (1995). A maximum test for scale: type 1 error rates and power. *Journal of Educational and Behavioral Statistics*. Spring 1995; **20(1)**: 27-39.
- CASELLA, G. AND M.T. WELLS (1996). Comparing p-values to Neyman-Pearson tests. In: *Bayesian Analysis in Statistics and Econometrics*. Edit by D.A. Berry, K.M. Chaloner and J.K. Geweke. John Wiley, New York. **Cap. 43**: 507-14.
- COCHRAN, W.G. (1983). *Planning and analysis of observational studies*. L.E. Moses and F. Mosteller, eds. John Wiley . New York.
- COHEN, J. (1988) *Statistical power analysis for the behavioral sciences*. Academic Press. New York.570 p.
- DEGROOT, M.H. (1970). *Optimal statistical decisions*. McGraw Hill. New York. 489 p.
- GAVER JR, D.P. , D.DRAPER, P.K. GOEL, J.B.GREENHOUSE, L.V. HEDGES, C.N. MORRIS AND C. WATERNAUX (1992). *Panel on statistical issues and opportunities for research in the combination of information*. National Research Council. National Academic Press. Washington, D.C..217p.
- GIBBONS, J.D. AND J.W. PRATT (1975). P-values: interpretation and methodology. *The American Statistician*. **29(1)**: 20-25.
- GOODMAN, S.N. (1989). Meta-analysis and evidence. *Controlled Clinical Trials*. **10**: 188-204.
- HEDGES, L.V. AND I. OLKIN (1985). *Statistical methods for meta-analysis*. Academic Press, Inc. Boston. 369 p.
- HUNG, H.M.J., R.T. O'NEILL, P. BAUER, AND K. KOHNE (1997). The behavior of the p-value when the alternative hypothesis is true. *Biometrics* **53**: 11-22.
- MANTON, D.G., M.A. WOODBURY AND H.D. TOLLEY. (1994). *Statistical applications using fuzzy sets*. John Wiley. New York. 312p.
- OAKES, M. (1993). The logic and role of meta-analysis in clinical research. *Statistical Methods in Medical Research*. **2**: 147-60.
- PETITTI, D.B. (2000). *Meta-analysis, decision analysis, and cost-effectiveness analysis: Methods for quantitative synthesis in Medicine*. Oxford Univ. Press. 306 p.
- ROMER, C. AND A. KANDEL (1995b). Fuzzy partitions of the sample space and fuzzy parameter hypothesis. *IEEE Transactions on Systems, Man and Cybernetics*. **25(9)**: 1314-22.
- SCHERVISH, M.J.(1996). P-values: what they are and what they are not. *The American Statistician*. **50(3)**: 203-206.
- WOODBURY, M.A.(1974). Clinical pure types as a fuzzy partition. *Journal of Cybernetics*. **4(3)**: 111-21.