Recent Developments in Multiple Comparison Procedures
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Appendix

New Horizons in Multiple Comparison Procedures

Outline of Lectures by Yosef Hochberg

1. *INTRODUCTION – AN EVOLUTIONARY PERSPECTIVE:* Multiple comparisons and multiplicity problems in the present practice of statistics, with special reference to biostatistical and biopharmaceutical research. Consequences of uncontrolled selection effects with special reference to the multiple subgroup problem.

2. *VISITING THE PAST FOR A BETTER VIEW OF THE NEW HORIZONS:* Pairwise comparisons in the cradle of multiple comparison procedures (MCPs) – the single factor ANOVA. The relevance of familywise error (FWE) rate control. The example of directional errors. Other areas of concern about simultaneous and selective inference: model selection, publication bias, exploratory data analysis and data mining.

3. *INTRODUCTION TO THE CLASSICAL APPROACH:* Basic notions of family and error rates. Union-Intersection and Intersection-Union procedures. Single step and step-wise procedures. A typology of problems and procedures.

4. *INTER-TREATMENT COMPARISONS:* Use and abuse of MCPs with ideas for amendments. Finite-intersection procedures. Single step procedures.

5. *EXTENSIONS OF SINGLE STEP PROCEDURES:* Unbalanced designs. Arbitrary correlations. Generalized linear models. New ideas on simple approximate ideas.

6. *EXTENDED AND IMPROVED STEPWISE PROCEDURES:* The closure method. When joint distributions are unknown. Using estimators of the number of true hypotheses.

7. *THE FALSE DISCOVERY RATE (FDR) APPROACH:* The FDR criterion. The non-adaptive procedure. The adaptive procedure. Summary of recent literature. FDR controlling MCPs for pairwise comparisons in a single factor design. Some ideas for further research.

8. *ON SOME MULTIPLICITY PROBLEMS IN CLINICAL TRIALS:* A review of multiplicity problems in clinical trials. The multiple endpoints problem. Primary and secondary endpoints. On the multiplicity of primary endpoints: An example with four primary endpoints. Subgroup analysis – incorporating logical constraints and correlations. What should be done when some tests are more important than others.

9. *QUESTIONS FROM THE PHARMACEUTICAL INDUSTRY:* Non-resolution problems in using the present required strategy for the Gold Standard Experiment (GSE). Some improved alternatives. Difficulties associated with present strategies in slow enrollment studies requiring an interim analysis only after an apriori specified number of subjects have entered the study. Preliminary results and future developments.

10. *INTRODUCTION TO POSTERIOR P-VALUES (PPV):* The MC problem is extended to include every problem of inference, which becomes specified only after data realization and/or "manipulation". A frequentist framework for PPV. Specific examples: dropouts in clinical trial and posterior meta analysis. The researcher who performed three almost significant experiments. Some semi-general philosophy and methods.