Introduction to Multiple Testing Adjustment

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Objectives:
In medical research, we often find it is very difficult to replicate the findings reported in the literature. The reasons for lack of replicability include false positive results, which can be caused by ignoring the issue of multiple testing. From this course, you will learn the methods to address the multiple testing issues and their applications in clinical trials and genetic epidemiology studies. (3G credits)

No required text book

Student Evaluation:
10% of the student’s evaluation is based on their class participation
30% of student’s evaluation will be based on assignments
60% of student’s evaluation will be based on an independent study (analyze and interpret publicly available dataset or develop a study protocol, which has multiple testing issue) and presentation at the end of the course.

1. Introduction (1-2 week)
   1.1. Motivation
   1.2. Error Rate Control

2. Multiple Testing Methods Based on Family-wise Error Control (3 weeks)
   2.1. Bonferroni and Weighted Bonferroni methods
   2.2. Fixed Sequence Test
   2.3. Fallback Methods and Extensions
   2.4. Holm and Weighted Holm Procedures
   2.5. Hochberg and Weighted Hochberg Procedures
   2.6. Gatekeeping Procedures
      2.6.1. Serial gatekeeping procedures
      2.6.2. Parallel gatekeeping procedures
      2.6.3. Mixture gatekeeping procedures
   2.7. Adaptive Alpha Allocation Approach (4A)
   2.8. Parametric Multiple Testing Methods
   2.9. Resampling-based Methods
   2.10. Monte Carlo Approach

3. Multiple Testing Methods Based on False Discovery Rate (FDR) Control (2 weeks)
   3.1. FDR and Weighted FDR Method
   3.2. FDR for Dependent Tests
3.3. Resample-based Methods
3.4. Monte Carlo Approach

4. Multiple Testing Adjustment in Clinical Trials (3-4 weeks)
  4.1. Analysis of Multiple Endpoints in Clinical Trials
  4.2. Comparisons of Multiple Treatment Effects
  4.3. Multiple Testing in Subgroups and Overall Population
  4.4. Multiple Testing in Studies with Adaptive Design

5. Multiple Testing Adjustment in Genetic Epidemiology Studies (3 week)
  5.1. Multiple Testing in Genome-Wide Association Study
  5.2. Multiple Testing in Analysis of Gene Expression Data
  5.3. Multiple Testing in Analysis of Methylation Data