Statistical tests for Rare Variants Data Rare Variants in Human Genetic Diseases: Comparison of Association Statistical Tests
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**Rare Variants in Human Genetic Diseases: Comparison of Association Statistical Tests**

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### Background and Objectives

GWASs allow to identify common genetic variants (CVs) associated with many common diseases. But these variants do not fully explain the heritability (i.e., proportion of phenotypic variance attributable to genetic variants).

**GWAS**

- **GWAS** aims to identify common genetic variants (CVs) associated with many common diseases.
- These CVs do not fully explain the heritability (proportion of phenotypic variance attributable to genetic variants).

**Summary of properties of the tests for RVs to be compared**

- Whether pooling over variants, using a MAI threshold to define RVs, sensitive to association directions (i.e.), whether possible use of weights, requiring permutations for p-value calculations and references for more details.

**Data**

- Genotypes and phenotypes generated as in (1), 6 main scenarios, sub-divided into 400 independent replicates, test significant level α = 5%, 500 permutations for association-based methods:
  - sample size 500 cases and 500 controls
  - 8 causal RVs, p = (0.48,16,32) non-causal RVs
  - p = 0.05 independent or p = 0.05 in Linkage Disequilibrium (LD)

**Pipeline of data creation and analysis**

1. After pre-processing, 871 samples (one per studied gene) were selected and the 324 patients in line.

**Results**

- The first dimension remains linked to:
  - all studied burden tests
  - kernel-based weighted adaptive C-Alpha test and BOMP.
- The second dimension explains the dimension of two non-burden tests:
  - C-Alpha and its kernelization "SKAT".

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### Material and Methods

#### Test Pool MAF threshold Sensitive weights Permut Refs

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### Reference