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Statistical methods for analysing complex genetic traits

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Stellingen

1. The ascertainment issue in family studies can be better addressed by conditioning on the set of probands relevant to ascertainment, rather than ignoring them and treating their relatives as if they were randomly selected.
This thesis, chapter 2
2. In the proband-family design estimating population parameters from the sample might lead to bias estimates. Parameters should be obtained from an available population based study.
This thesis, chapter 2
3. When the statistical model cannot be fully specified, the score test is a good alternative to its corresponding likelihood ratio test.
This thesis, chapter 4
4. Under the presence of more than one associated variant with the disease, a test statistic that takes the maximum of individual statistics over the possible variants has low power. A test statistic that sums over the possible variants has good power and it should be preferred.
This thesis, chapters 4 and 5
5. Statistics developed to test a specific alternative hypothesis are more privileged to detect this alternative if it is true.
6. Genome wide association studies are promising tools for detecting common variants responsible for complex genetic traits. Rare disease variants will only be detected when they have large effects.
7. Despite rapidly decreasing genotyping costs, genome wide association studies are still expensive, as they need genotyping hundreds of thousands of SNPs for large samples. To further lower the study costs while maintaining good power, a multiple stage design should be used.
8. "To consult a statistician after an experiment is finished is often merely to ask him to conduct a post-mortem examination. He can perhaps say what the experiment died of" R.A. Fisher, 1938.