

WCN GENESTAT
Workpackage on Biostatistics
Technical Report 2002-12-31

1. General

GeneStat continues to review the recent statistical literature (including software) on genetic association analysis. A "user-friendly" review will be posted on the GeneStat internet portal by Fall 2003. A comparison will be made of a number of likelihood and Bayesian estimation based software packages which are publicly available for haplotype estimation. We have focused in particular on (i) haplotype analysis and written software for fitting models to case-control data which include gene-environment interaction and allows the analysis of comorbidity, the association of two disorders, which occurs commonly with complex diseases (Humphreys). Other areas include (ii) efficient algorithms for handling large incomplete data problems (Humphreys) (iii) properties of statistical tests and estimation (including power issues) in genetic association studies when ascertainment is based on extreme quantitative trait values (Palmgren, Humphreys) and (iv) statistical issues related to the use of pooled DNA (Humphreys, Palmgren), (v) design and analyses of longitudinal twin studies accounting for dropout and death (Palmgren, Ripatti).

2. Terms of contract

(i) Establishment of an Internet portal:

In accordance with the contract, the StatGene internet portal was built by Stathouse Ltd in May-September 2002 and is available on

<http://jazzhouse.stathouse.fi/genestat/genestat.htm>

Tutorials will be supplied by mid-2003, together with a bulletin board/ mailing list for methodology and software related questions. The time table and content is in accordance with the contract.

(ii) Statistical Consulting for Biobanking:

GeneStat has given advice on statistical issues related to the design and analyses of genetic association studies to: CGB, KI (Brookes, Gu), IMM, KI (DeFaire), BioScience, Huddinge, KI (Kere), Uppsala Clinical Research, UCR (Berglund, Syvänen), Umeå Center for Molecular Medicine, UCMM (Holmberg, Andersson). In addition the Biostatistics Group at the Dept of Medical Epidemiology is involved with statistical issues related to the Swedish Twin Registry (Pedersen), the Swedish Multigenerational Registry (Ekbom) and the KIChip facility for cDNA micro-array analyses (Reimers). In terms of statistical consulting the WCN contract has been fulfilled.

(iii) Workshop on Biostatistical Aspects of Biobanking:

In September 2002 the GeneStat scientists (Palmgren, Humphreys) organized a workshop on 'Statistical Haplotype Reconstruction', with Lon Cardon (Cambridge, UK), David Clayton (Oxford, UK) and Nan Laird (Harvard, US) as invited speakers. A sequel under the WCN auspices will be organized in October 2003, at which the internet learning network/portal will be presented.

3. Publications

Gu, H.F., Abutaiti, A., Östensson, C-G, **Humphreys, K.**, Wahlestedt, C., Efendic, S., Brookes, A.J. Single Nucleotide Polymorphisms in the Adiponectin (APM1) Gene confer genetic risk for impaired glucose tolerance (IGT) and Type 2 Diabetes in Swedish Caucasians. To be submitted to Human Molecular Genetics.

Humphreys, K. Estimating haplotype phase from population-based case-control study data and association analysis of comorbidity. Manuscript in preparation.

Humphreys, K. and Wedren, S. (2002). Efficient estimation of haplotype phase for case-control data. Contributed paper, International Biometric Conference, Freiburg, Germany. (Abstract).

Pawitan, Y., Bjöhle, J., Wedren, S., **Humphreys, K.**, Skoog, L., Huang, F., Amler, L., Shaw, P., Hall, P., Bergh, J. Gene expression profiling for prognosis using Cox regression. To be submitted to Biostatistics.

Sara Wedren, S., Lovmar, L., **Humphreys, K.**, Magnusson, C., Melhus, H., Kindmark, A., Landegren, U., Lagerström-Ferme, R., Stiger, F., Persson, I., Baron, J., Weiderpass, E. Polymorphism in the estrogen receptor alpha gene is associated to breast cancer risk. Submitted to Journal of the National Cancer Institute.

Ripatti S, Gatz M, Pedersen NL, **Palmgren J.** A three-state frailty model for age at onset of dementia and death in Swedish twins. Genetic Epidemiology in press

Grünewald M., Pedersen N., Arner P, Brookes T., **Palmgren J.** Linkage disequilibrium mapping using a case-control design and continuous phenotype measurements. Contributed paper, International Biometric Conference, Freiburg, Germany. (Abstract).

Dominicus A., **Ripatti S.**, Pedersen N. L., **Palmgren J.** Modeling cognitive ability from longitudinal data with dropout and death. Contributed paper, International Biometric Conference, Freiburg, Germany. (Abstract).

Pedersen NL, **Ripatti S**, Berg S, Reynolds C, Hofer SM, Finkel D, Gatz M, **Palmgren J.** The Influence of Mortality on Twin Models of Change. In press.

4. Economic review

A partial review as of Sept 2002 (Ebba Grönberg, MEP):

Salaries: 308.6 kkr

Ripatti (100% Jan-March 2002) Genetic association studies

Humphreys (40% Jan-Aug 2002) Genetic association studies

Nordlund (109 hrs) Administration

Other:

Conference, IBC, Freiburg (Humphreys, oral contribution) 15.6 kkr

Stathouse inc. Internet Portal 58.4 kkr

Overhead 52.3 kkr

Total (Sept 2002) 435 kkr

A full economic review for 2002 will be provided by Jan 31, 2003.

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