Author's response to reviews

Title: A comparison of genomic profiles of complex diseases under different models

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Dear Editor-in-Chief,

Please find enclosed the manuscript “A comparison of genomic profiles of complex diseases under different models”, which we would like to be considered for publication in BMC Medical Genomics.

The main aim of this work was to understand what are the possibilities and limitations of predictive models of individual risk to complex diseases based on genome-wide data sets. For this purpose we performed a wide study of different approaches, already used or new, regarding (1) the algorithms used to learn the model (from classic genetic risk scores to the state-of-the-art methods in the Machine Learning field, such as support vector machines, bagging algorithms or boosting algorithms), (2) the structure of the input variable used to build the models (genotypes versus haplotypes), (3) the threshold imposed to select model variables and, for the haplotype-based models, (4) the genetic model (additive, recessive and dominant). We conducted the study on 7 complex diseases (WTCCC) with different heritability and prevalence values.

We believe at least two interesting results have shed some light in this research field. The first one is related to the approach with highest performance when predicting risk in two lowly polymorphic diseases (type 1 diabetes and rheumatoid arthritis): a boosting algorithm and how its robustness to redundant variables (something very common in GWAS due to linkage disequilibrium) seems to be the reason it outperformed all the other algorithms. The second, in agreement with other studies, refers to a lack of success when predicting risk in highly polymorphic diseases, such as hypertension, type 2 diabetes or coronary artery disease).

The authors declare that they have no competing interests.

Thank you for your consideration,

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