A Comparison of Genetic Risk Score Models for Predictive Modeling of Disease Risk

Ronglin Che*, North Carolina State University
Alison Motsinger-Reif, North Carolina State University

Abstract

A priority in genetic epidemiology is to identify susceptible variants for common diseases and further construct a feasible statistical model(s) to predict the disease risk with these variants. However, most of the variants convey a relatively modest effect and thus the application of the disease predictive models built on single variants is limited in clinical utility. Thus, developing methods to construct valid and effective risk profiles is a priority. In the current study, we compare four previously proposed genetic risk score functions and present a new function, including a simple risk score summary of risk alleles, several weighted risk score functions and polygenic risk score models. We perform a case-control simulation study under a wide range of potential multi-locus genetic models of disease, and demonstrate the relative performance of each of the methods that may provide guidance in informing researchers about choosing methods under different scenarios. Weighted methods including odds ratio or minor allele frequency are recommended if effect size varies greatly. A simple count risk score is preferable if sample size is small and no strong prior information is available.

Keywords: Simple count Genetic Risk Score; Weighted Genetic Risk Score; Polygenic; Disease predictive modeling; Effect size.

* Presenting author