Abstract:
The rapid acceleration of whole-genome sequencing and densely-imputed genotyping array data collection in biomedical settings has resulted in the rise of genetic compendiums filled with rich longitudinal disease data. One common feature of these datasets is a plethora of interval-censored outcomes. However, few tools are available for the analysis of genetic datasets with interval-censored outcomes, and in particular, there is a lack of methodology available for set-based inference, which is used to associate genes with outcomes. This work develops three such tests for interval-censored settings beginning with a variance components test for interval-censored outcomes, the interval censored sequence kernel association test (ICSKAT). We also provide the interval-censored version of the Burden test, and then we integrate ICSKAT and Burden to construct the interval censored sequence kernel association test - optimal (ICSKATO) combination. These tests unlock set-based analysis of interval-censored datasets with analogs of three highly popular set-based tools commonly applied to continuous and binary outcomes. The proposed approaches are applied to the investigation that motivated this study, an examination of the genes associated with bone mineral density deficiency and fracture risk.