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**A COMPARISON BETWEEN METHYLATION RISK SCORES USED**

**TO PREDICT ALCOHOL USE**

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Several studies have developed Methylation Risk Scores (MRSs) to predict alcohol consumption, however, the overlap in CpGs between MRSs has not been examined. Most MRSs are developed using LASSO or Elastic Net Regression that select only one CpG site from regions with many highly correlated sites. Hence, there is a high likelihood that these MRSs may capture overlapping signals. To investigate this, we first annotated CpGs that form 5 different alcohol MRSs to examine both positional and genic overlap. The Corrected Cover Area (CCA) method was used to quantify the overlap in individual sites between the three MRSs based on Generation Scotland, sites for the Liu and Xiaoyu MRSs which utilized the 450K array, and gene overlap between all 5 MRSs. The highest overlap was the genic overlap between Lohoff and McCartney at 13.037% while the highest CpG overlap was between Lohoff and McCartney at 8.39%. A permuted Fisher’s Exact Test was computed for each pair of MRSs within the three sets of comparisons. All tests were significant (p-value ≤ 1x10-4) suggesting a significant overlap in both position and genes for all examined MRS pairs. However, it is unclear if this overlap is due to all MRSs predicting alcohol consumption, or if it is due to the same cohorts being used in some MRSs. Future studies should utilize independent cohorts to disentangle potential cohort specific effects and may also investigate overlaps on a regional level.

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