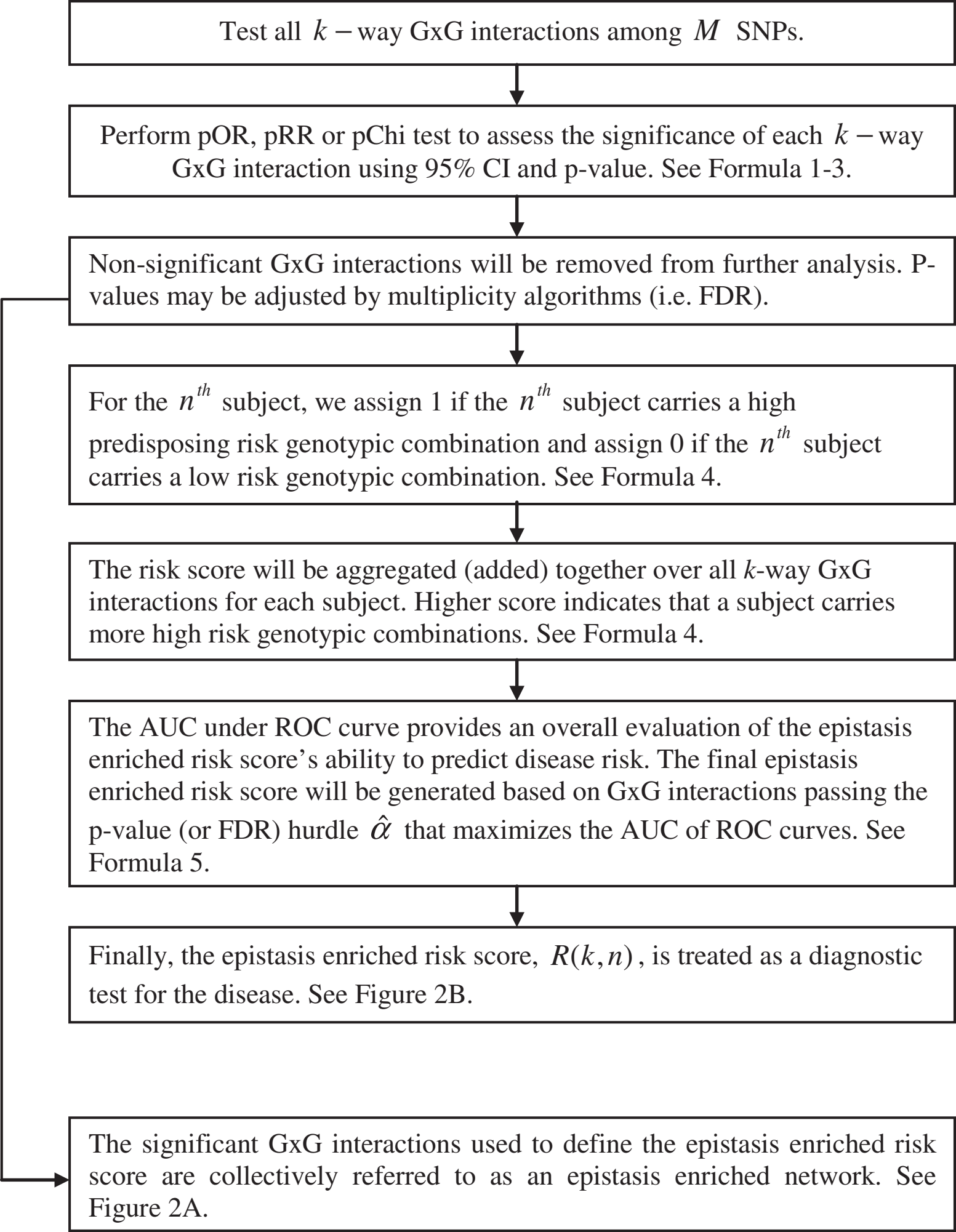
Test all $k-$way GxG interactions among M SNPs.
Perform pOR, pRR or pChi test to assess the significance of each $k-$way GxG interaction using 95% CI and p-value. See Formula 1-3.
Non-significant GxG interactions will be removed from further analysis. P-values may be adjusted by multiplicity algorithms (i.e. FDR).
For the n^{th} subject, we assign 1 if the n^{th} subject carries a high predisposing risk genotypic combination and assign 0 if the n^{th} subject carries a low risk genotypic combination. See Formula 4.
The risk score will be aggregated (added) together over all *k*-way GxG interactions for each subject. Higher score indicates that a subject carries more high risk genotypic combinations. See Formula 4.
The AUC under ROC curve provides an overall evaluation of the epistasis enriched risk score's ability to predict disease risk. The final epistasis enriched risk score will be generated based on GxG interactions passing the p-value (or FDR) hurdle $\hat{\alpha}$ that maximizes the AUC of ROC curves. See Formula 5.
Finally, the epistasis enriched risk score, $R(k,n)$, is treated as a diagnostic test for the disease. See Figure 2B.
The significant GxG interactions used to define the epistasis enriched risk score are collectively referred to as an epistasis enriched network. See Figure 2A.