Start with a total of \( m \) SNPs.

Perform the ReliefF algorithm on \( m \) SNPs. Sort \( m \) SNPs by ReliefF scores in an ascending order.

Generate p-values for the exhaustive search of \( k \)-way interactions among a total of \( m \) SNPs using the original or extended MDR methods.

Let \( m_1 \) be the number of remaining SNPs. At the beginning, \( m_1 = m \).

Perform the global test on \( \binom{m_1}{k} \) p-values regarding all \( k \)-way interactions among \( m_1 \) remaining SNPs.

Test

\[ H_0 : P \sim \text{Uniform}(0,1) \text{ vs.} \]
\[ H_a : \text{Pr}(P \leq p) > p \text{ for } p \in (0,1). \]

If the global test fails to reject \( H_0 \), then
- remove one SNP with the lowest ReliefF score;
- let \( m_1 = m - 1 \);
- let \( m = m_1 \).

If the global test rejects \( H_0 \), then
- p-values shift towards 0 (Pattern 2 in Figure 1);
- the optimal number of SNPs for the final MDR analysis is \( m_1 \).

Perform the final MDR analysis on the \( m_1 \) remaining SNPs.