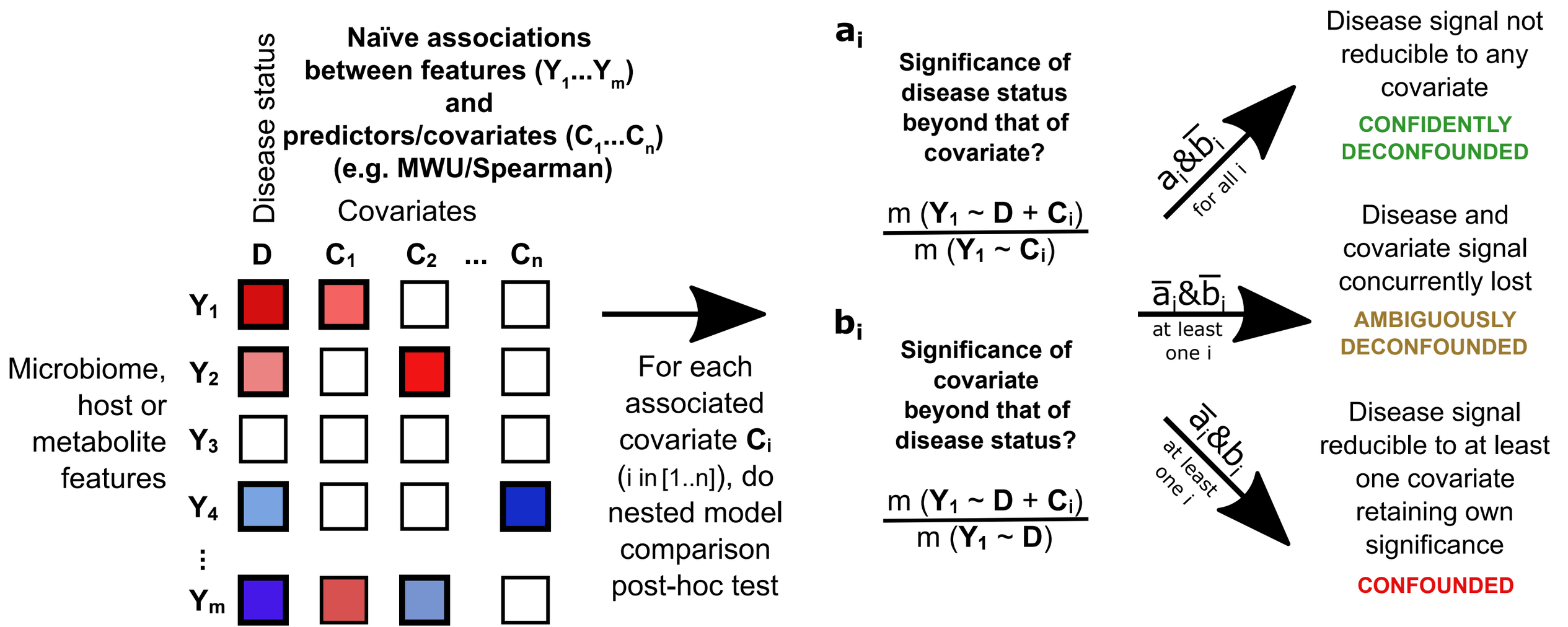
Naïve associations between features (Y_1...Y_m) and predictors/covariates (C_1...C_n) (e.g. MWU/Spearman)
Disease status
Covariates
D
C_1
C_2
...
C_n
Y_1
Y_2
Y_3
Y_4
Y_m
Microbiome, host or metabolite features
For each associated covariate C_i (i in [1..n]), do nested model comparison post-hoc test
a_i
Significance of disease status beyond that of covariate?
$\frac{m\ (Y_1 \sim D + C_i)}{m\ (Y_1 \sim C_i)}$
b_i
Significance of covariate beyond that of disease status?
$\frac{m\ (Y_1 \sim D + C_i)}{m\ (Y_1 \sim D)}$
$a_i \& \bar{b}_i$ for all i
Disease signal not reducible to any covariate
CONFIDENTLY DECONFOUNDED
$\bar{a}_i \& \bar{b}_i$ at least one i
Disease and covariate signal concurrently lost
AMBIGUOUSLY DECONFOUNDED
$\bar{a}_i \& b_i$ at least one i
Disease signal reducible to at least one covariate retaining own significance
CONFOUNDED