Multiple Testing in a Two-Stage Adaptive Design with Combination Tests Controlling FDR

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1 Supplementary Materials

1.1 Exponentially Decreasing Effect Sizes

To examine the performance of proposed procedures in a more complicated genetic mode, we explored a model with exponentially decreasing effect sizes. (i) We generated two independent sets of $m = 1000$ uncorrelated random variables $Z_i \sim N(\mu_i, 1), i =$

$1, ..., m$, one for Stage 1 and the other for Stage 2, with $m\pi_0$ of these μ_i's being set at zero and the rest at equally spaced exponentially decreasing effect sizes at $1.5 \times (2^2, 2^1, 2^{0.5}, 2^0)$. (ii) We then tested $H_i : \mu_i = 0$ against $H_i : \mu_i > 0$, simultaneously for $i = 1, ..., m$, by applying each of the following procedures to the generated data: The (alternative versions of) BH-TSADC and Plug-In BH-TSADC procedures at level α, each with both Fisher's and Simes' combination functions, the level α first-stage and full-data BH procedures. For our two-stage procedures, the early acceptance boundary λ' was set at 0.5 and the early rejection boundary λ was set at 0.005, 0.010, and 0.025. (iii) We noted the false discovery proportion and the proportion of false nulls that are rejected. We repeated steps (i)-(iii) 1000 times and average out the above proportions over these 1000 runs to obtain the final simulated values of FDR and average power (the expected proportion of false nulls that are rejected) for each of these procedures.

Figures 1 and 2 show that in the setting with the exponentially decreasing effect sizes at $1.5 \times (2^2, 2^1, 2^{0.5}, 2^0)$, the power differences between our suggested procedures and the BH procedure applied to the first stage data and full data from both stages is decreasing compared to that in the setting with the constant effect size at 2.

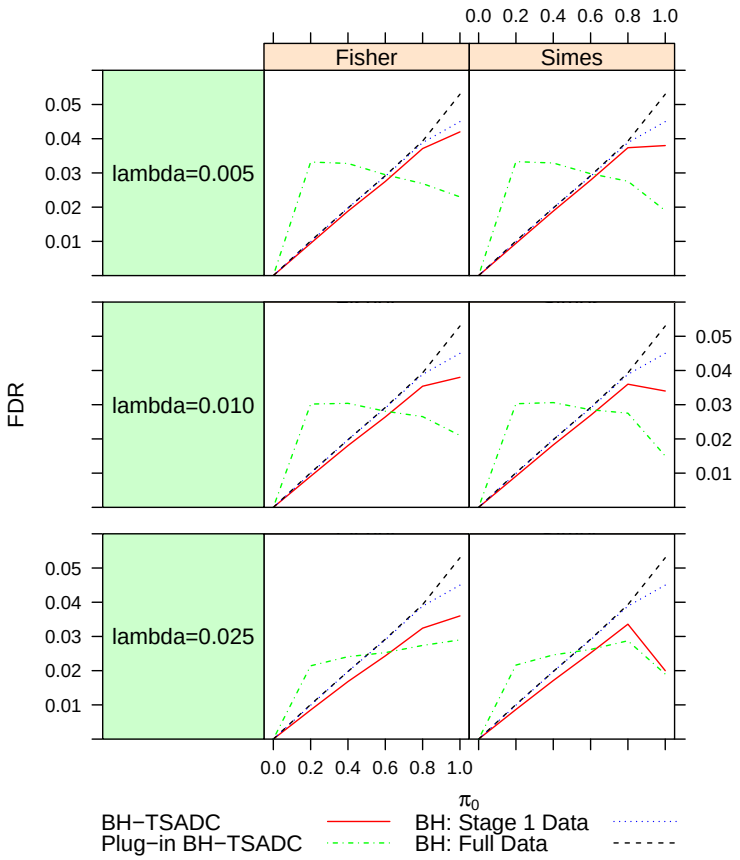

Figure 1: Simulated FDRs of BH-TSADC and Plug-In BH-TSADC procedures based on both Fisher's and Simes' combination functions, with $m = 1000$, equally spaced exponential decreasing effect sizes $1.5 \times (2^2, 2^1, 2^{0.5}, 2^0)$, $\lambda = 0.005, 0.010$, and 0.025, and $\lambda' = 0.5$, compared to simulated FDRs of the first-stage and full-data BH procedures, at $\alpha = 0.05$.

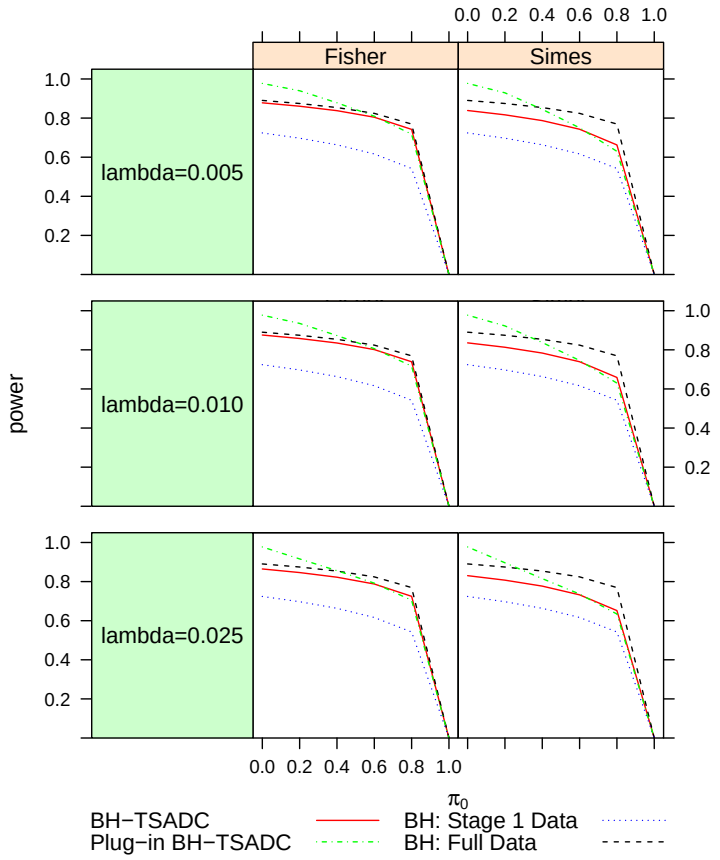

Figure 2: Simulated average powers of BH-TSADC and Plug-In BH-TSADC procedures based on both Fisher's and Simes' combination functions, with $m = 1000$, equally spaced exponential decreasing effect sizes $1.5 \times (2^2, 2^1, 2^{0.5}, 2^0)$, $\lambda = 0.005, 0.010$, and 0.025, and $\lambda' = 0.5$, compared to simulated average powers of the first-stage and full-data BH procedures, at $\alpha = 0.05$.