

What You See is What You Get

Methodological Component

Collin Nolte

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- Mean structure assumptions
- Alternative methods
 - Modified bootstrap
 - Permutation test
- FWER control
- Power

Mean Assumptions

Observed data:

$$y_{it} = f(t|\theta_i) + \epsilon_{it}$$

Homogeneous Means

For all subjects i, j in group $g = 1, \dots, G$,

$$\theta_i = \theta_j$$

Heterogeneous Means

Subject i in group $g = 1, \dots, G$ follows

$$\theta_i \sim N(\mu_g, V_g)$$

with no presumption that $\theta_i = \theta_j$

Heterogeneous Bootstrap

Differs from original bootstrap in that it samples subjects with replacement

This gives distribution for the b th bootstrap estimate in group g

$$\theta_{bg}^{(het)} \sim N \left(\mu_g, \frac{1}{n_g} V_g + \frac{1}{n_g^2} \sum s_i^2 \right)$$

This compares with homogeneous bootstrap which samples without replacement,

$$\theta_{bg}^{(hom)} \sim N \left(\mu_g, \frac{1}{n_g^2} \sum s_i^2 \right).$$

Heterogeneous Bootstrap

The change in algorithm (and resulting distribution) are only things that change

Still construct test statistic

$$T_t = \frac{(\bar{p}_{1t} - \bar{p}_{2t})}{\sqrt{s_{1t}^2 + s_{2t}^2}}$$

at each time point, with FWER being controlled with modified Bonferroni adjustment

Permutation Test

Begin by constructing test statistic on observed data,

$$T_t^{(p)} = \frac{|\bar{p}_{1t} - \bar{p}_{2t}|}{\sqrt{s_{1t}^2 + s_{2t}^2}}$$

Then proceed similarly to a standard permutation test by permuting labels for group membership at each permutation. At each permutation, retain the maximum test statistic, giving a null distribution of P values denoted \tilde{T}

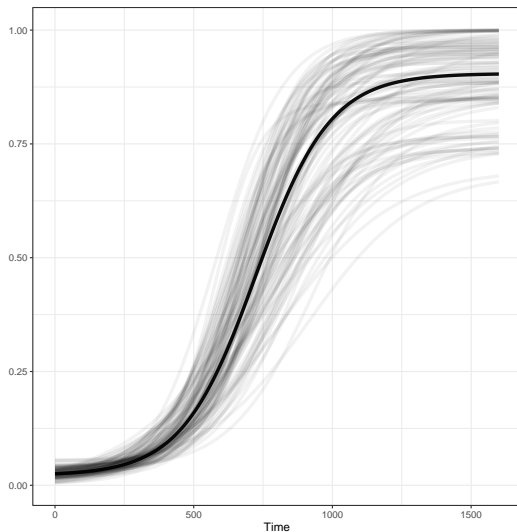
Letting \tilde{T}_α be the $1 - \alpha$ quantile of \tilde{T} , significant regions will be those in which

$$T_t^{(p)} \geq \tilde{T}_\alpha$$

FWER Simulation

- Logistic function from 0-1600
- With and without $AR(1)$ error
- For heterogeneous means, sampled from empirical distribution from VWP with NH subjects
- Paired data only for heterogeneous means, subjects differed only in error term
- 25 subjects in each group (50 total), 100 simulations

FWER Simulation



FWER Results (Unpaired)

| $\theta_i = \theta_j$ | AR Error | AR(1) Specified | Hom Bootstrap | Het Bootstrap | Permutation |
|-----------------------|-------------|--------------------|------------------|------------------|-------------|
| No | Yes | Yes | 0.06 | 0.01 | 0.08 |
| No | Yes | No | 0.87 | 0.08 | 0.00 |
| No | No | Yes | 0.08 | 0.00 | 0.06 |
| No | No | No | 0.15 | 0.02 | 0.01 |
| Yes | Yes | Yes | 0.92 | 0.03 | 0.05 |
| Yes | Yes | No | 0.96 | 0.02 | 0.08 |
| Yes | No | Yes | 0.99 | 0.05 | 0.03 |
| Yes | No | No | 1.00 | 0.05 | 0.06 |

Table 1: FWER for empirical parameters (unpaired)

FWER Results (Paired)

| $\theta_i = \theta_j$ | AR Error | AR(1) Specified | Hom Bootstrap | Het Bootstrap | Permutation |
|-----------------------|-------------|--------------------|------------------|------------------|-------------|
| Yes | Yes | Yes | 0.49 | 0.02 | 0.01 |
| Yes | Yes | No | 0.94 | 0.03 | 0.02 |
| Yes | No | Yes | 0.72 | 0.02 | 0.00 |
| Yes | No | No | 0.74 | 0.04 | 0.00 |

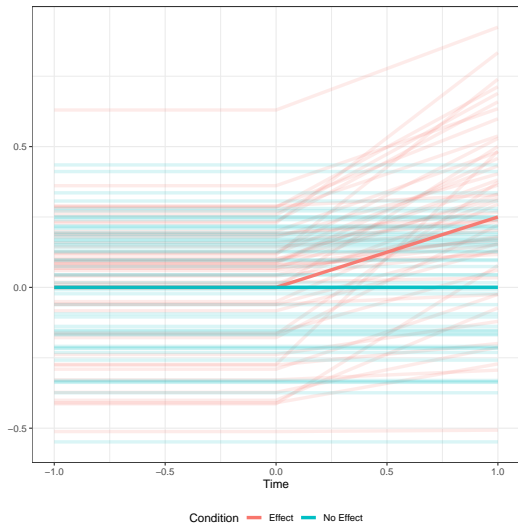
Table 2: FWER for empirical parameters (paired)

- Fit using piecewise function

$$y = \begin{cases} b & x < 0 \\ mx + b & x \geq 0 \end{cases}$$

- cases with AR specification ugh
- I have other sims that just aren't presented
- 25 subjects in each group, 1000 simulations
- Metrics include FWER, family wise type II error, and a distribution of where differences first detected (explain)

Power Simulation

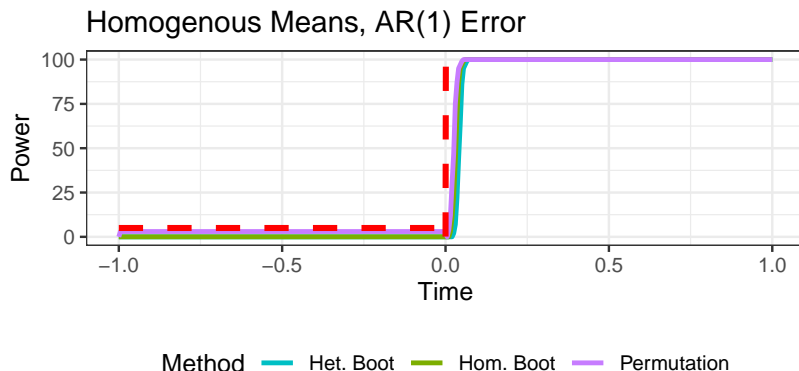


Power Results

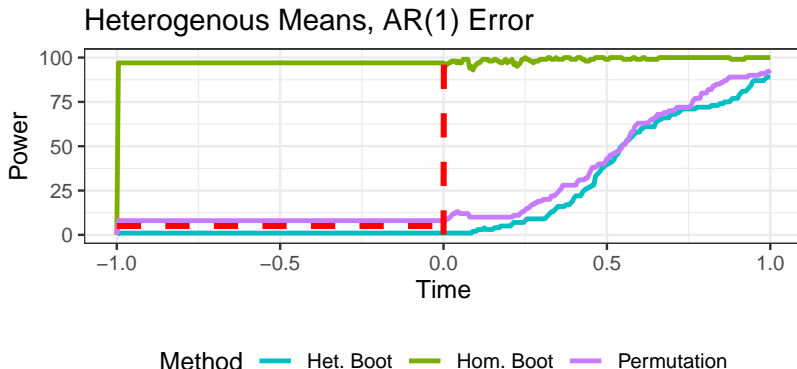
| Method | Het. | AR(1) | α | β | $1 - \alpha - \beta$ | 1st Qu. | Median | 3rd Qu. |
|-----------|------|-------|----------|---------|----------------------|---------|--------|---------|
| Hom. Boot | No | Yes | 0.00 | 0.00 | 1.00 | 0.025 | 0.030 | 0.035 |
| Het. Boot | No | Yes | 0.00 | 0.00 | 1.00 | 0.035 | 0.040 | 0.045 |
| Perm | No | Yes | 0.03 | 0.00 | 0.97 | 0.015 | 0.025 | 0.025 |
| Hom. Boot | Yes | No | 0.96 | 0.00 | 0.04 | 0.005 | 0.008 | 0.010 |
| Het. Boot | Yes | No | 0.00 | 0.10 | 0.90 | 0.403 | 0.513 | 0.690 |
| Perm | Yes | No | 0.03 | 0.05 | 0.92 | 0.378 | 0.515 | 0.681 |
| Hom. Boot | Yes | Yes | 0.97 | 0.00 | 0.03 | 0.008 | 0.010 | 0.010 |
| Het. Boot | Yes | Yes | 0.01 | 0.10 | 0.89 | 0.420 | 0.525 | 0.690 |
| Perm | Yes | Yes | 0.08 | 0.03 | 0.89 | 0.360 | 0.540 | 0.705 |

Table 3: Power for methods

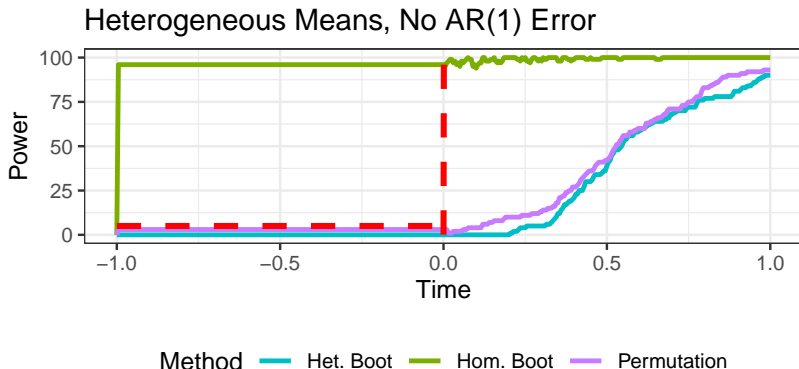
Power (Homogeneous Means)



Power (Heterogeneous Means, AR(1))



Power (Heterogeneous Means, No AR(1))



Conclusions

- New methods adequately control FWER under myriad of situations
- Also have comparable power under homogeneous means assumptions
- In general, permutation performs closest to nominal α while having slightly improved power (compared to heterogeneous bootstrap)
- Sampling without replacement will be removed from `bdots` package as there is no situation in which it drastically outperforms any of the other two