

## INTRODUCTION

- Clustered data are observed in various domains.
- Units within a cluster are correlated while units between clusters are independent.  
Example: in dental studies, individuals are clusters and teeth in an individual are units within a cluster.
- Informative intra-cluster group size (IICGS) [1, 2] : Outcomes from a group in a cluster can be associated with the no. of units belonging to that group in that cluster.
- There does not exist a statistical method to test the existence of IICGS in a clustered data.
- We propose a bootstrap based hypothesis testing of IICGS in clustered data - assuming exchangeability within groups in a cluster [3].
- Through simulation studies, we show that our method can accurately detect IICGS in clustered data.

## METHODOLOGY

$M$  = No. of clusters  
 $B$  = No. of bootstrap samples  
 $Y_{ik}$  =  $k^{th}$  observation in the  $i^{th}$  cluster  
 $N_i$  = No. of observations in the  $i^{th}$  cluster.  
 $N_{i0}$  = No. of observations of group 0 in the  $i^{th}$  cluster  
 $N_{i1}$  = No. of observations of group 1 in the  $i^{th}$  cluster.  
 $G_{ik}$  = Group membership indicator.  
 $V_i = \{N_i, Y_{ik}, G_{ik}\}, k = 1, \dots, N_i, i = 1, \dots, M$

•  $H_0: \hat{F}(y) = \tilde{F}(y)$  vs.  $H_1: \hat{F}(y) \neq \tilde{F}(y)$

where  $\hat{F}(y) = \frac{\sum_{i=1}^M \sum_{k=1}^{N_i} I(Y_{ik} \leq y, G_{ik}=d)}{\sum_{i=1}^M \sum_{k=1}^{N_i} I(G_{ik}=d)}$  and  
 $\tilde{F}(y) = \frac{\sum_{i=1}^M \frac{1}{2N_{id}} \sum_{k=1}^{N_i} I(Y_{ik} \leq y, G_{ik}=d)}{\sum_{i=1}^M \frac{1}{2N_{id}} \sum_{k=1}^{N_i} I(G_{ik}=d)}$ ; where  $d = 0, 1$  [1]

- Test statistics:

$$1) T_F = \sup_y |\hat{F}(y) - \tilde{F}(y)|$$

$$2) T_{CM} = \sum_{k \in \mathcal{J}} [k M_k \int (\hat{F}_k(y) - \tilde{F}(y))^2 dy]$$

where  $\mathcal{J}$ : set of unique cluster size,

$M_k$ : no. of clusters of size  $k$ ,

$\hat{F}_k(y) = \frac{1}{K M_k} \sum_{i=1}^M \sum_{j=1}^{N_i} \mathbb{I}(N_i = k, Y_{ij} \leq y)$ : estimator of the distribution of cluster size  $k$  [3].

## Algorithm

➤ **Step 1:** Test statistic  $T = T(V)$ , where  $V = (V_1, \dots, V_M)$ .

➤ **Step 2:** Consider  $j^{th}$  bootstrap sample,  $j = 1, \dots, B$ .

- Permute the units in each group within a cluster.
- Resample  $M$  clusters from the permuted data set by repeating for every  $i = 1, \dots, M$ .
  - Draw a random cluster  $V$  with index  $i^*$  from  $\{1, \dots, M\}$ .
  - If  $(N_{i^*1} \geq N_{i1}) \cap (N_{i^*0} \geq N_{i0})$  then the bootstrap

$$\text{cluster is } V_{ji}^* = \begin{cases} N_{i1}; Y_{i^*1}^{(1)}, \dots, Y_{i^*N_{i1}}^{(1)} \\ N_{i0}; Y_{i^*0}^{(0)}, \dots, Y_{i^*N_{i0}}^{(0)} \end{cases}$$

where  $\{Y_{i1}^{(1)}, \dots, Y_{iN_{i1}}^{(1)}\}$  and  $\{Y_{i0}^{(0)}, \dots, Y_{iN_{i0}}^{(0)}\}$  represent the observations of the group 1 and group 0, respectively.

- If  $(N_{i^*1} \geq N_{i1}) \cap (N_{i^*0} < N_{i0})$  then the bootstrap cluster is merged from two matching clusters;

$$V_{ji}^* = \begin{cases} N_{i1}; Y_{i^*1}^{(1)}, \dots, Y_{i^*N_{i1}}^{(1)} \\ N_{i0}; Y_{i^*0}^{(0)}, \dots, Y_{i^*N_{i0}}^{(0)}, Y_{k0(N_{i^*0}+1)}^{(0)}, \dots, Y_{k0N_{i0}}^{(0)} \end{cases}$$

where  $k0 = \text{argmin}_{k0} (D_0(V_{i^*0}, V_{k0}): N_{k0} \geq N_{i0})$

- If  $(N_{i^*0} \geq N_{i0}) \cap (N_{i^*1} < N_{i1})$  then the bootstrap cluster is merged from two matching clusters;

$$V_{ji}^* = \begin{cases} N_{i0}; Y_{i^*0}^{(0)}, \dots, Y_{i^*N_{i0}}^{(0)} \\ N_{i1}; Y_{i^*1}^{(1)}, \dots, Y_{i^*N_{i1}}^{(1)}, Y_{k1(N_{i^*1}+1)}^{(1)}, \dots, Y_{k1N_{i1}}^{(1)} \end{cases}$$

where  $k1 = \text{argmin}_{k1} (D_1(V_{i^*1}, V_{k1}): N_{k1} \geq N_{i1})$

- If  $(N_{i^*1} < N_{i1}) \cap (N_{i^*0} < N_{i0})$  then the bootstrap cluster is merged from two matching clusters;

$$V_{ji}^* = \begin{cases} N_{i1}; Y_{i^*1}^{(1)}, \dots, Y_{i^*N_{i1}}^{(1)}, Y_{k1(N_{i^*1}+1)}^{(1)}, \dots, Y_{k1N_{i1}}^{(1)} \\ N_{i0}; Y_{i^*0}^{(0)}, \dots, Y_{i^*N_{i0}}^{(0)}, Y_{k0(N_{i^*0}+1)}^{(0)}, \dots, Y_{k0N_{i0}}^{(0)} \end{cases}$$

- $j^{th}$  bootstrap sample:  $V_j^* = (V_{j1}^*, \dots, V_{jM}^*)$  and test statistic:  $T_j^* = T(V_j^*)$ .

➤ **Step 3:** Compute the  $p$ -value as  $\frac{1}{B} \sum_{j=1}^B \mathbb{I}(T_j^* \geq T)$ .

Note: The distance between two clusters is defined as:

$$D_1(V_{i1}, V_{j1}) = (\min\{N_{i1}, N_{j1}\})^{-1} \sum_{k1=1}^{\min\{N_{i1}, N_{j1}\}} (Y_{i1k1}^{(1)} - Y_{j1k1}^{(1)})^2$$

$$D_0(V_{i0}, V_{j0}) = (\min\{N_{i0}, N_{j0}\})^{-1} \sum_{k0=1}^{\min\{N_{i0}, N_{j0}\}} (Y_{i0k0}^{(0)} - Y_{j0k0}^{(0)})^2$$

For tied distances, choose one of the clusters at random.

## RESULTS

### Simulation studies

- $M = 50$  and 100 clusters,  $B = 500$  and 1000 bootstrap samples and 500 Monte Carlo iterations.
- Test statistics for group 0 are  $T_{F0}, T_{CM0}$ , and for group 1 are  $T_{F1}, T_{CM1}$ .
- Let  $Y_{i1} = 0.5 + a_i + e_1$  and  $Y_{i0} = 0.5 + a_i + e_0$  where  $a_i \sim N(0,1)$ ; where  $a_i$  = random cluster effect  $e_1 \sim N(0,0.3)$  and  $e_0 \sim N(0.01,0.3)$ ,  $i = 1, 2, \dots, M$

➤ **Empirical size calculation**

$$(N_{i1}-1) \sim \text{Poi}(15), (N_{i0}-1) \sim \text{Poi}(12)$$

- Nominal size = 0.05

M	B	T <sub>F0</sub>	T <sub>CM0</sub>	T <sub>F1</sub>	T <sub>CM1</sub>
50	500	0.050	0.090	0.060	0.076
	1000	0.050	0.088	0.072	0.076
100	500	0.062	0.114	0.058	0.090
	1000	0.064	0.112	0.058	0.092

Table 1: Empirical sizes

➤ **Power calculation**

$$(N_{i1}-1) \sim \text{Poi}(15(\exp(\gamma a_i))), (N_{i0}-1) \sim \text{Poi}(12(\exp(\gamma a_i)))$$

$$\gamma = 0.1, 0.2, 0.3, 0.4, 0.5$$

M	B	T <sub>F0</sub>	T <sub>CM0</sub>	T <sub>F1</sub>	T <sub>CM1</sub>
50	500	0.522	0.262	0.654	0.342
	1000	0.524	0.282	0.650	0.342
100	500	0.834	0.496	0.902	0.556
	1000	0.834	0.504	0.906	0.566

Table 2: Statistical power when  $\gamma = 0.1$

## CONCLUSIONS

- Our bootstrap based nonparametric hypothesis testing for IICGS detection is robust in terms of being free from any distributional assumptions.
- Our method, based on TF statistic, maintains the type-1 error rate (size) at the target level of 0.05.
- Our test has high power under a variety of simulation settings. The power increases with the increase in the number of clusters.
- In future, we plan to extend our method to account for covariate(s) in addition to the grouping factor.

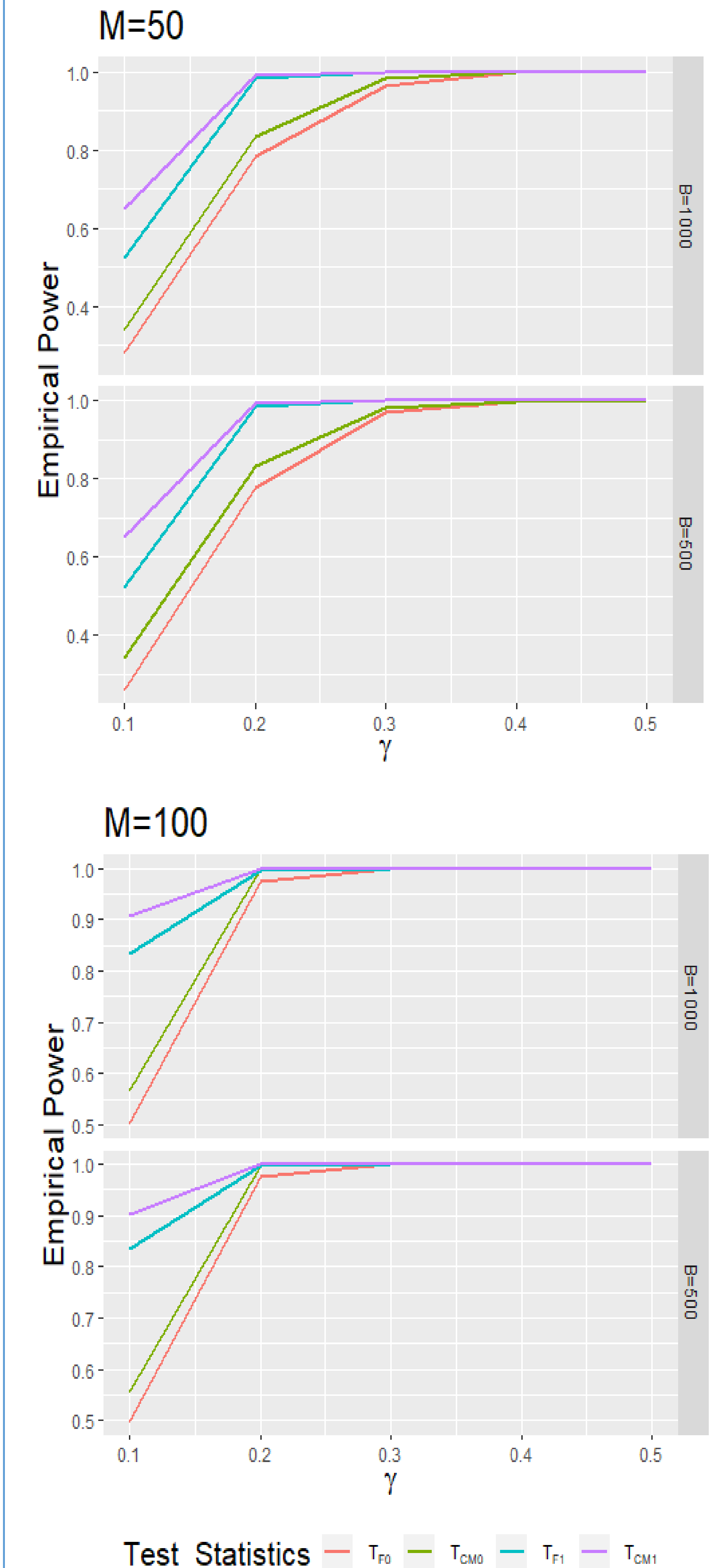


Figure 1: Power curves for different choices of M

## REFERENCES

- [1] Dutta S, Datta S. *Biometrics*. 2016;72:432–40.
- [2] Dutta S, Datta S. *Stat. Med.* 2018;72:4807–22.
- [3] Nevalainen J, Oja H, Datta S. *Stat. Med.* 2017; 36:2630-40.