

Resampling Techniques and their Application

-Class 10-

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Example

- Panic disorder longitudinal trial

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 - Specific physical exercise therapy

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 - $n = 15$ patients

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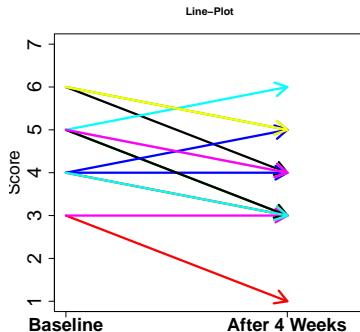
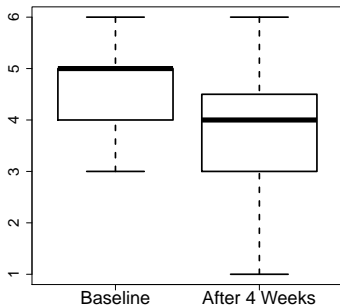
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 - Response: CGI-score **before and after** 4 weeks of treatment

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- What is the research question?

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- What is the data scale?
- Are means appropriate?

Statistical Model

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 - Other options?

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 $5,5,3,4,5)$

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```

```
y=c(4,1,3,4,6,3,3,4,3,3,  
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```

```
xM<-median(x)
```

```
xY<-median(y)
```

```
theta<- xM-xY
```

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 - $\theta = \text{Median}(X) - \text{Median}(Y)$
 - Crude Measure
 - What else could we measure?

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```
#X<Y +1/2(X=Y)
```

```
grid1=expand.grid(x,y)
prop1 = (grid1[,1]<grid1[,2]) +
1/2*(grid1[,1]==grid1[,2])
p=mean(prop1)
p
```

```
#Y<X+1/2(X=Y)
prop2 = (grid1[,2]<grid1[,1]) +
1/2*(grid1[,2]==grid1[,1])
q=mean(prop2)
q
p+q
```


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 - Interpretation
 - If $p < \frac{1}{2}$: X tends to be larger than Y
 - If $p = 1/2$: No tendency to smaller or larger values
 - Hypothesis:

$$H_0 : p = 1/2$$

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Relative Effects: Other Examples

- Two samples: What is the chance, data in the first are smaller than in the second?
- What is the probability that men are taller than women?
- What is the probability, blood pressure under treatment is higher than under control?
- What is the probability, that scores after 4 weeks of treatment are smaller than at the beginning?
- **The relative effect thus measures, whether scores are smaller/larger between the groups**

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Rel. Effect: Point Estimator

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- Sort the data
- Smallest number gets rank 1, largest gets rank $2n$
- Mid-ranks are used to adjust for ties
- In R: `rank(x)`

```
x <-c(5,3,2,1,4)
rank(x)
```

Two samples:

```
x=c(6,3,5,4,5,3,4,5,5,4,
6,4,4,5,6)
```

```
y=c(4,1,3,4,6,3,3,4,3,3,
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```

```
xy=c(x,y)
rank(xy)
```

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- Compute

$$\bar{R}_{x\cdot} = \frac{1}{n} \sum_{k=1}^n R_{xk} \quad \text{"Mean of the first"}$$

$$\bar{R}_{y\cdot} = \frac{1}{n} \sum_{k=1}^n R_{yk} \quad \text{"Mean of the second"}$$

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$$\hat{p} = \frac{1}{2n} (\bar{R}_{y\cdot} - \bar{R}_{x\cdot}) + 1/2$$

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```
n<-length(x)
```

```
xy<-c(x,y)
```

```
rx<-rank(x)
```

```
mRx <-mean(rx[1:n])
```

```
mRy <-mean(rx[(n+1):(2*n)])
```

```
phat<-1/(2*n)*(mRy-mRx)+1/2
```

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$$Z_{xk} = \frac{1}{n} * (R_{xk} - R_{xk}^{(x)})$$

$$Z_{yk} = \frac{1}{n} * (R_{yk} - R_{yk}^{(y)})$$

$$D_k = Z_{xk} - Z_{yk}$$

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```
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```

```
rx<-rank(x)
```

```
ry<-rank(y)
```

```
rx<-rank(x)
```

```
ry<-rank(y)
```

```
Z1k <- 1/n*(rx[1:n]-rx)
```

```
Z2k <- 1/n*(ry[(n+1):(2*n)]-ry)
```

```
Dk <- Z1k-Z2k
```

```
sigmahat <-var(Dk)
```


Test Procedures: Munzel's Test

- Test Statistic

$$T = \sqrt{n} \frac{(\hat{p} - 1/2)}{\hat{\sigma}}$$

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$$\hat{p} \pm t_{1-\alpha/2}(n-1) \hat{\sigma} / \sqrt{n}$$

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```
T=sqrt(n)*(phat-1/2)/sqrt(sigmahat)
pvalue=2*min(pt(T,n-1),1-pt(T,n-1))
```

```
crit <-qt(0.975,n-1)
SE <- sqrt(sigmahat)/sqrt(n)
```

```
Lower = phat -crit*SE
Upper = phat +crit*SE
```

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- Is the method applicable when samples are small?

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- Type-1 error simulation ($\alpha = 5\%$, $n_{sim} = 10,000$)

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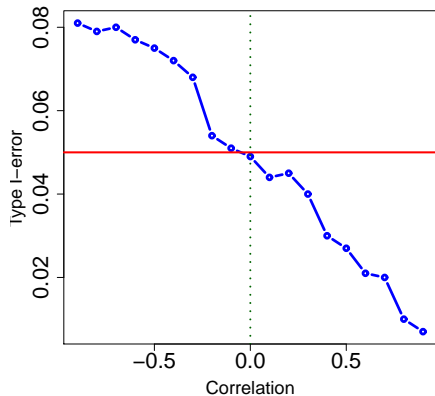
- Type-1 error simulation ($\alpha = 5\%$, $n_{sim} = 10,000$)
- $\mathbf{X}_k = (X_{1k}, X_{2k}) \sim N(\mathbf{0}, \mathbf{V})$, $k = 1, \dots, 10$

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- $\mathbf{X}_k = (X_{1k}, X_{2k}) \sim N(\mathbf{0}, \mathbf{V})$, $k = 1, \dots, 10$
- \mathbf{V} : compound symmetric (variance = 1, covariance = ρ)

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 - Repeat this step several times
 - CI: $\hat{p} \pm z_{1-\alpha/2}^* \hat{\sigma} / \sqrt{n}$

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 - **Permute randomly X_{1k} and X_{2k} within each pair X_k**
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- Project: Explore other resampling methods

Improve Munzel's Test

- How?
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- Note: Permuting data overall is not applicable in this model

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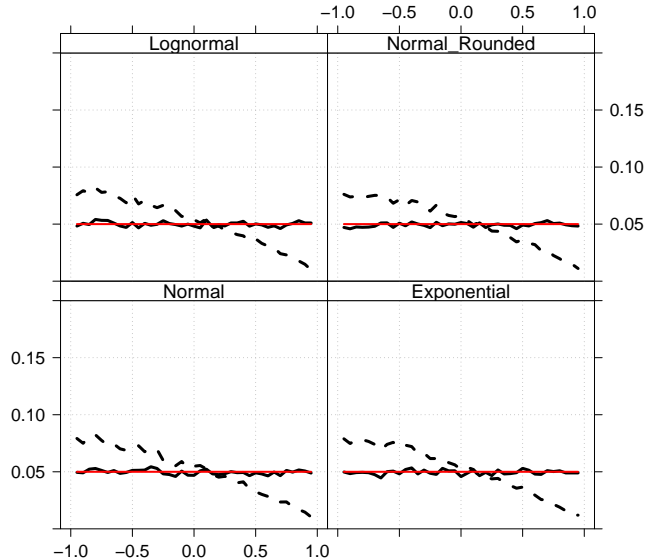
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 - Reference: Konietzschke and Pauly (2012), A studentized permutation test for the Nonparametric Behrens-Fisher Problem in Paired Data

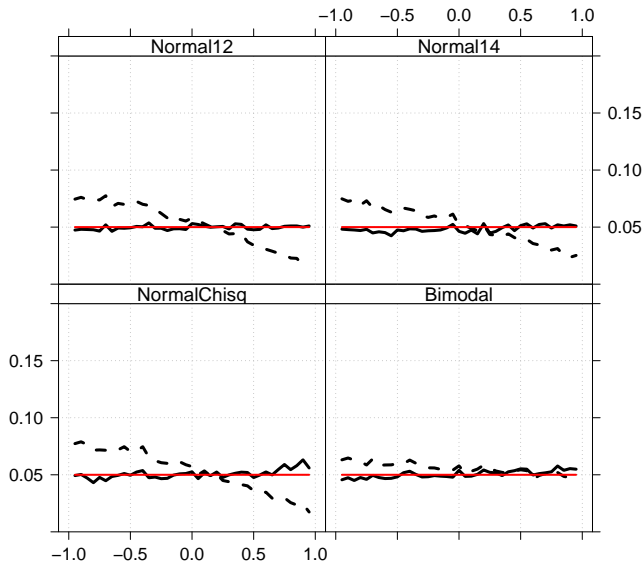
Simulations - Exchangeable data

Type - I Error = 5% (n=10)



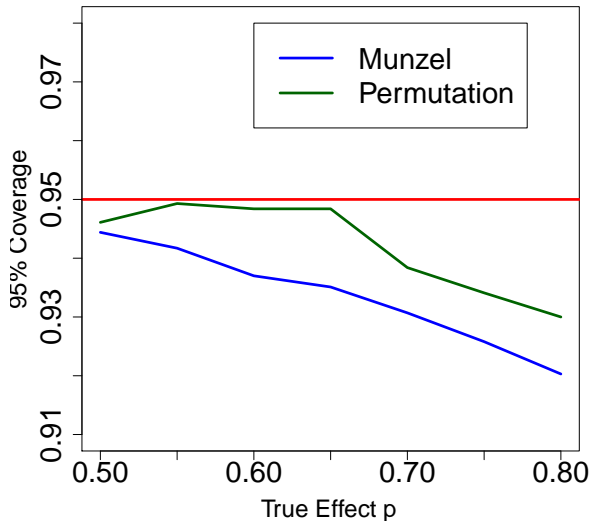
Simulations - Non Exchangeable data

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Simulations - 95%-Coverage Probability

n=7; bivariate normal with rho=0



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- Hypothesis $H_0 : p = 1/2 \rightarrow p - value = .0006$
- 95%-CI: $[0.16; 0.43]$
- Munzel's test: similar results

Patient	PGI		Ranks	
k	Baseline	Week 4	Baseline	Week 4
1	6	4	28.5	14.0
2	3	1	5.5	1.0
3	5	3	22.5	5.5
4	4	4	14.0	14.0
5	5	6	22.5	28.5
6	3	3	5.5	5.5
7	4	3	14.0	5.5
8	5	4	22.5	14.0
9	5	3	22.5	5.5
10	4	3	14.0	5.5
11	6	5	28.5	22.5
12	4	5	14.0	22.5
13	4	3	14.0	5.5
14	5	4	22.5	14.0
15	6	5	28.5	22.5

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$$\mathbf{X}_k = (X_k, X_{k+n})', k = 1, \dots, n$$

- $n = 3$

$$\mathbf{X}_k = \begin{pmatrix} X_1 & X_4 \\ X_2 & X_5 \\ X_3 & X_6 \end{pmatrix} \Rightarrow \mathbf{X}_k = (X_1, X_2, X_3, X_4, X_5, X_6)'$$

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 -

Implementation- III

 $n=4$ [illegible]


```

permuall<-function(nsim, rho, n){
#-----Daten einlesen-----#
n1<-n+1
n2<-2*n
x<-matrix(0, ncol=nsim, nrow=n2)
for (h in 1:nsim){
x11<-rnorm(n)
x22<-rho*x11+sqrt(1-rho^2)*(rnorm(n))
x[,h]<-c(x11,x22)}

#-----Brunner-Munzel test-----#
tcrit<-qt(0.975,n-1)
x1<-x[1:n,]
x2<-x[n1:n2,]
rx<-apply(x, 2, rank)
rx1<-rx[1:n,]
rx2<-rx[n1:n2,]
rix1<-apply(x1, 2, rank)
rix2<-apply(x2, 2, rank)
BM1<-1/n*(rx1-rix1)
BM2<-1/n*(rx2-rix2)
BM3<-BM1-BM2
BM4<-1/(2*n)*(rx1 - rx2)
pd<-colMeans(BM2)
m<-colMeans(BM3)
v<-(colSums(BM3^2)-n*m^2)/(n-1)
v0<-(v==0)
v[v0]<-1/n
T<-sqrt(n)*(pd-1/2)/sqrt(v)

```

```
#-----Studentized Permutation Test---#
```

```
nperm<-2^n
```

```
if(nperm <10000){
```

```
  p<-0
```

```
  for (i in 1:n){
```

```
    a<-rep(c(rep(c(i,i+n),nperm/(2^i)),rep(c(i+n,i),nperm/(2^i)))),2^(i-1))
```

```
    p<-rbind(p,a)
```

```
  }
```

```
  p<-p[2:(n+1),]
```

```
  P<-matrix(p,ncol=nperm)}
```

```
if (nperm >=10000){
```

```
  nperm=10000
```

```
  P<-matrix(0,nrow=(2*n),ncol=nperm)
```

```
  for (h in 1:nperm){
```

```
    P[,h]<-c(t(apply(cbind(1:n,(n+1):(2*n)),1,sample))))}}
```

```

#-----Beginn der Simulationsschleife----#
BM=PERM=c()
for (s in 1:nsim){
  xs<-x[,s]
  rs<-rx[,s]
  #-----Permutationstest-----#
  xperm<-matrix(xs[P],nrow=n2,ncol=nperm)
  rxperm<-matrix(rs[P],nrow=n2,ncol=nperm)
  xperm1<-xperm[1:n,]
  xperm2<-xperm[n1:n2,]
  rxperm1<-rxperm[1:n,]
  rxperm2<-rxperm[n1:n2,]
  riper1<-apply(xperm1,2,rank)
  riper2<-apply(xperm2,2,rank)
  BMperm2<-1/n*(rperm2-riper2)
  BMperm3<-1/n*(rperm1-riper1)-BMperm2
  pdperm<-colMeans(BMperm2)
  mperm3<-colMeans(BMperm3)
  vperm3<-(colSums(BMperm3^2)-n*mperm3^2)/(n-1)
  vperm30<-(vperm3==0)
  vperm3[vperm30]<-1/n
  Tperm<-sqrt(n)*(pdperm-1/2)/sqrt(vperm3)
  p1perm<-mean(Tperm<=T[s]); p2perm<-mean(Tperm>=T[s])
  pperm<-2*min(p1perm,p2perm)
  PERM[s]<-(pperm<0.05)}
  ergebnis<-data.frame(nsim=nsim,
    nperm=nperm,n=n,rho=rho,BM= mean(abs(T)>t crit),
    PERM=mean(PERM))
  ergebnis}
permua11(100,0,7)

```