A Handbook of Statistical Analyses Using R

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CHAPTER 3

Conditional Inference: Guessing Lengths, Suicides, Gastrointestinal Damage, and Newborn Infants

3.1 Introduction

3.2 Conditional Test Procedures

3.3 Analysis Using R

3.3.1 Estimating the Width of a Room Revised

The unconditional analysis of the room width estimated by two groups of students in Chapter ?? lead to the conclusion that the estimates in metres are slightly larger than the estimates in feet. Here, we reanalyse these data in a conditional framework. First, we convert metres into feet and store the vector of observations in a variable y:

```R
R> data("roomwidth", package = "HSAUR")
R> convert <- ifelse(roomwidth$unit == "feet", 1, 3.28)
R> feet <- roomwidth$unit == "feet"
R> metre <- !feet
R> y <- roomwidth$width * convert
```

The test statistic is simply the difference in means:

```R
R> T <- mean(y[feet]) - mean(y[metre])
R> T

[1] -8.858893
```

In order to approximate the conditional distribution of the test statistic $T$ we compute 9999 test statistics for shuffled $y$ values. A permutation of the $y$ vector can be obtained from the `sample` function.

```R
R> meandiffs <- double(9999)
R> for (i in 1:length(meandiffs)) {
+     sy <- sample(y)
+     meandiffs[i] <- mean(sy[feet]) - mean(sy[metre])
+ }
```

The distribution of the test statistic $T$ under the null hypothesis of independence of room width estimates and groups is depicted in Figure 3.1. Now, the value of the test statistic $T$ for the original unshuffled data can be compared
Approximated conditional distribution of the difference of mean roomwidth estimates in the feet and metres group under the null hypothesis. The vertical lines show the negative and positive absolute value of the test statistic $T$ obtained from the original data.

with the distribution of $T$ under the null hypothesis (the vertical lines in Figure 3.1). The $p$-value, i.e., the proportion of test statistics $T$ larger than 8.859 or smaller than -8.859 is

```R
R> greater <- abs(meandiffs) > abs(T)
R> mean(greater)
[1] 0.00740074
```

with a confidence interval of

```R
R> binom.test(sum(greater), length(greater))$conf.int
```
Note that the approximated conditional p-value is roughly the same as the p-value reported by the t-test in Chapter 2.

```
R> library("coin")
R> independence_test(y ~ unit, data = roomwidth,
+                   distribution = exact())
```

```
Exact General Independence Test
data: y by unit (feet, metres)
Z = -2.5491, p-value = 0.008492
alternative hypothesis: two.sided
```

**Figure 3.2** R output of the exact permutation test applied to the `roomwidth` data.

```
R> wilcox_test(y ~ unit, data = roomwidth,
+              distribution = exact())
```

```
Exact Wilcoxon-Mann-Whitney Test
data: y by unit (feet, metres)
Z = -2.1981, p-value = 0.02763
alternative hypothesis: true mu is not equal to 0
```

**Figure 3.3** R output of the exact conditional Wilcoxon rank sum test applied to the `roomwidth` data.

### 3.3.2 Crowds and Threatened Suicide

```
R> data("suicides", package = "HSAUR")
R> fisher.test(suicides)
```

```
Fisher's Exact Test for Count Data
data: suicides
p-value = 0.0805
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 0.7306872 91.0288231
sample estimates:
odds ratio
6.302622
```

**Figure 3.4** R output of Fisher’s exact test for the `suicides` data.
3.3.3 Gastrointestinal Damages

Here we are interested in the comparison of two groups of patients, where one group received a placebo and the other one Misoprostol. In the trials shown here, the response variable is measured on an ordered scale – see Table ??.

Data from four clinical studies are available and thus the observations are naturally grouped together. From the data.frame Lanza we can construct a three-way table as follows:

R> data("Lanza", package = "HSAUR")
R> xtabs(~ treatment + classification + study, data = Lanza)

, , study = I

<table>
<thead>
<tr>
<th></th>
<th>classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>treatment</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>21 2 4 2 0</td>
</tr>
<tr>
<td>Placebo</td>
<td>2 2 4 9 13</td>
</tr>
</tbody>
</table>

, , study = II

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>treatment</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>20 4 6 0 0</td>
</tr>
<tr>
<td>Placebo</td>
<td>8 4 9 4 5</td>
</tr>
</tbody>
</table>

, , study = III

<table>
<thead>
<tr>
<th></th>
<th>classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>treatment</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>20 4 3 1 2</td>
</tr>
<tr>
<td>Placebo</td>
<td>0 2 5 5 17</td>
</tr>
</tbody>
</table>

, , study = IV

<table>
<thead>
<tr>
<th></th>
<th>classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>treatment</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>1 4 5 0 0</td>
</tr>
<tr>
<td>Placebo</td>
<td>0 0 0 4 6</td>
</tr>
</tbody>
</table>

For the first study, the null hypothesis of independence of treatment and gastrointestinal damage, i.e., of no treatment effect of Misoprostol, is tested by

R> library("coin")
R> cmh_test(classification ~ treatment, data = Lanza, +    scores = list(classification = c(0, 1, 6, 17, 30)), +    subset = Lanza$study == "I")

Asymptotic Linear-by-Linear Association Test
data: classification (ordered) by treatment (Misoprostol, Placebo)
ANALYSIS USING R

\[ Z = -5.371, \ p-value = 7.83 \times 10^{-8} \]
alternative hypothesis: two.sided

and, by default, the conditional distribution is approximated by the corresponding limiting distribution. The \( p \)-value indicates a strong treatment effect.

For the second study, the asymptotic \( p \)-value is a little bit larger

\[ R> \text{cmh_test}(\text{classification} \sim \text{treatment}, \ \text{data} = \text{Lanza}, + \text{scores} = \text{list}(\text{classification} = c(0, 1, 6, 17, 30)), + \text{subset} = \text{Lanza}\$\text{study} == "II") \]

Asymptotic Linear-by-Linear Association Test

data: \ classification (ordered) by \ treatment (Misoprostol, Placebo)
Z = -3.4733, \ p-value = 0.000514
alternative hypothesis: two.sided

and we make sure that the implied decision is correct by calculating a confidence interval for the exact \( p \)-value

\[ R> \ p \leftarrow \text{cmh_test}(\text{classification} \sim \text{treatment}, \ \text{data} = \text{Lanza}, + \text{scores} = \text{list}(\text{classification} = c(0, 1, 6, 17, 30)), + \text{subset} = \text{Lanza}\$\text{study} == "II", \text{distribution} = + \text{approximate}(\text{B} = 19999)) \]

\[ R> \text{pvalue}(p) \]
[1] \ <5.00025e-05
99 percent confidence interval:
0.000000000 0.000264894

The third and fourth study indicate a strong treatment effect as well

\[ R> \text{cmh_test}(\text{classification} \sim \text{treatment}, \ \text{data} = \text{Lanza}, + \text{scores} = \text{list}(\text{classification} = c(0, 1, 6, 17, 30)), + \text{subset} = \text{Lanza}\$\text{study} == "III") \]

Asymptotic Linear-by-Linear Association Test

data: \ classification (ordered) by \ treatment (Misoprostol, Placebo)
Z = -5.3065, \ p-value = 1.118 \times 10^{-7} \]
alternative hypothesis: two.sided

\[ R> \text{cmh_test}(\text{classification} \sim \text{treatment}, \ \text{data} = \text{Lanza}, + \text{scores} = \text{list}(\text{classification} = c(0, 1, 6, 17, 30)), + \text{subset} = \text{Lanza}\$\text{study} == "IV") \]

Asymptotic Linear-by-Linear Association Test

data: \ classification (ordered) by \ treatment (Misoprostol, Placebo)
Z = -3.9675, \ p-value = 7.262 \times 10^{-5} \]
alternative hypothesis: two.sided

At the end, a separate analysis for each study is unsatisfactory. Because the design of the four studies is the same, we can use \text{study} as a block variable and perform a global linear-association test investigating the treatment effect
of Misoprostol in all four studies. The block variable can be incorporated into
the formula by the | symbol.

R> cmh_test(classification ~ treatment | study, data = Lanza,
+   scores = list(classification = c(0, 1, 6, 17, 30)))

Asymptotic Linear-by-Linear Association Test

data: classification (ordered) by
treatment (Misoprostol, Placebo)
stratified by study
Z = -9.1443, p-value < 2.2e-16
alternative hypothesis: two.sided

Based on this result, a strong treatment effect can be established.

3.3.4 Teratogenesis

In this example, the medical doctor (MD) and the research assistant (RA)
assessed the number of anomalies (0, 1, 2 or 3) for each of 395 babies:

R> anomalies <- c(235, 23, 3, 0, 41, 35, 8, 0,
+   20, 11, 11, 1, 2, 1, 3, 1)
R> anomalies <- as.table(matrix(anomalies,
+   ncol = 4, dimnames = list(MD = 0:3, RA = 0:3)))
R> anomalies

<table>
<thead>
<tr>
<th>RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD</td>
</tr>
<tr>
<td>----</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

We are interested in testing whether the number of anomalies assessed by
the medical doctor differs structurally from the number reported by the research
assistant. Because we compare paired observations, i.e., one pair of measure-
ments for each newborn, a test of marginal homogeneity (a generalisation of
McNemar’s test, see Chapter 2) needs to be applied:
R> mh_test(anomalies)

Asymptotic Marginal Homogeneity Test

data:  response by
       conditions (MD, RA)
     stratified by block
   chi-squared = 21.227, df = 3, p-value = 9.446e-05

The $p$-value indicates a deviation from the null hypothesis. However, the levels of the response are not treated as ordered. Similar to the analysis of the gastrointestinal damage data above, we can take this information into account by the definition of an appropriate score. Here, the number of anomalies is a natural choice:

R> mh_test(anomalies, scores = list(response = c(0, 1, 2, 3)))

Asymptotic Marginal Homogeneity Test for Ordered Data

data:  response (ordered) by
       conditions (MD, RA)
     stratified by block
   Z = -4.5847, p-value = 4.545e-06
alternative hypothesis: two.sided

In our case, one can conclude that the assessment of the number of anomalies differs between the medical doctor and the research assistant.