BIOS 662

Homework 4 Solution

October, 2018

Question 1

The data come from pairs of children (a PKU case and his/her normal sibling). Because the children in a pair are siblings, they cannot be regarded as independent. So it is not appropriate to conduct two-sample tests. Instead, we conduct one-sample tests on the difference between the IQ test scores within each sibling pair.

(a) Let Y_i denote the IQ of the PKU case minus that of his/her normal sibling in pair i. If IQ is normally distributed, then the IQ of the differences is also normally distributed, so it may be reasonable to assume that $Y_1, \ldots, Y_n$ are iid with $Y_i \sim N(\mu, \sigma^2)$, for some μ and σ^2, where μ is the mean difference in IQ between a PKU case and his/her closest-age normal sibling.

Hypotheses: $H_0 : \mu = 0$ versus $H_A : \mu \neq 0$. (A one-sided alternative may also be reasonable, if we think there is no chance the dietary therapy could be so effective as to reverse the direction of association.)

(b) Assuming that the Y_i are normally distributed but that σ^2 is unknown, we use a one-sample t-test. Here $n = 21$, so

$$C_\alpha = \{t : |t| > t_{n-1,1-\alpha/2}\} = \{t : |t| > t_{20,0.975}\} = \{t : |t| > 2.086\}$$

Now

$$t = \frac{\bar{Y} - \mu_0}{s/\sqrt{n}} \sim t_{n-1} = \frac{-6.05 - 0}{11.612/\sqrt{21}} = -2.39.$$

Because $|-2.39| = 2.39 > 2.086$, we reject H_0 and conclude that the dietary therapy does not eliminate the IQ gap between cases and their siblings.

Also $p = 2 \cdot \Pr(t_{20} \leq -2.39) = 0.027$.

Using R:

```
> t.test(iq.diff)

        One Sample t-test

data:  iq.diff
t = -2.3866, df = 20, p-value = 0.027
alternative hypothesis: true mean is not equal to 0
95 percent confidence interval:
 -11.3335159  -0.7617221
sample estimates:
mean of x
-6.047619
```

Using SAS:

```
proc ttest;
   var iq_diff;

The TTEST Procedure

Variable:  iq_diff

  N        Mean     Std Dev     Std Err     Minimum     Maximum

 21     -6.0476     11.6124      2.5340    -33.0000     20.0000

    Mean       95% CL Mean        Std Dev      95% CL Std Dev

 -6.0476    -11.3335  -0.7617     11.6124      8.8842  16.7691

    DF    t Value    Pr > |t|

    20      -2.39      0.0270
```

(c) A 95% CI for μ is

$$\bar{Y} \pm t_{n-1,1-\alpha/2} \cdot s/\sqrt{n} = -6.05 \pm 2.086 \cdot 11.612/\sqrt{21} = (-11.33, -0.76).$$

This agrees with the results in R and SAS.

(d) Even with dietary therapy, on average a child with PKU has significantly lower IQ at age 4-6 than his or her closest-age normal sibling. The mean IQ of children with PKU who are on the dietary therapy in this study is 6.05 points lower than that of their normal siblings.

(e) Assumptions are that IQ data are normally distributed, that the difference between IQs of pairs all come from the same normal distribution (with the same mean and variance), and that the difference in IQ for any pair is independent of that for any other pair.

(f) Let $\zeta_{0.5}$ denote the median of the differences in IQ between children with PKU and their closest-age normal siblings. Then $H_0 : \zeta_{0.5} = 0$ and $H_A : \zeta_{0.5} \neq 0$.

To determine the critical region we need to find the largest $r_{\alpha/2}$ for which

$$\Pr[R \leq r_{\alpha/2} \mid H_0] = \frac{1}{2^n} \sum_{i=0}^{r_{\alpha/2}} \binom{n}{i} \leq \frac{\alpha}{2}$$

Using R

```
> 2*sum(dbinom(0:5,21,0.5))
[1] 0.0266037

> 2*sum(dbinom(0:6,21,0.5))
[1] 0.07835388
```

Confirming using the SIGN.test function:

```
> SIGN.test(iq.diff)

        One-sample Sign-Test

data:  iq.diff
s = 6, p-value = 0.07835
alternative hypothesis: true median is not equal to 0
```

So $r_{\alpha/2} = 5$ and thus $C_{0.05} = \{0,1,2,3,4,5,16,17,18,19,20,21\}$

In this dataset, $r =$ (number of observations > 0) $= 6 \notin C_{0.05}$ so we cannot reject H_0 and we conclude that the data are consistent with the IQ of the PKU cases being similar to that of their normal siblings. Also, $p = 2 \cdot \Pr(r \leq 6) = 0.078 > 0.05$. Using R:

```
> 2*pbinom(6,21,0.5)
[1] 0.07835388
```

(g) In part (d) we rejected the null hypothesis that the mean difference is zero whereas in (f) we did not reject the null hypothesis that the median difference is 0. When the data are approximately normally distributed the t test can be more powerful than the sign test — the gain in power is because of the additional assumption (normality).

Question 2

Here there is no link between any particular hypertensive and normotensive subjects. So the two samples should be independent and thus two-sample tests should be used.

I argue below for the Wilcoxon test. If you make a reasonable argument for the assumptions of the t-test, it is okay to use it. Below is SAS code for the t-test and corresponding edited output. As with the Wilcoxon test, we would not reject H_0, which in this case is that the mean sodium intake is the same in the two groups.

```
proc ttest;
 class group;
 var sodium;

Variable:  sodium

group           N      Mean   Std Dev   Std Err   Minimum   Maximum

Hypertensive   15    1931.3     490.0     126.5    1100.0    2720.0
Normal         12    1690.0     430.0     124.1    1000.0    2375.0
Diff (1-2)            241.3     464.5     179.9

Method           Variances        DF    t Value    Pr > |t|

Pooled           Equal            25       1.34      0.1918
Satterthwaite    Unequal      24.744       1.36      0.1856

              Equality of Variances

Method      Num DF    Den DF    F Value    Pr > F

Folded F        14        11       1.30    0.6720
```

My preference is to use the Wilcoxon rank sum test here for the following reasons. First, based on the histograms in Figure 1, the sodium intakes in the two groups do not appear to be normally distributed. Second, based on the empirical distribution functions and the boxplots in Figure 1, the assumption of a location shift made by the rank sum test does seem to be plausible.

Let group 1 be the Hypertensive subjects and group 2 the Normal subjects, with sample sizes $n_1 = 15$ and $n_2 = 12$, respectively. Denote the corresponding distribution functions by F_1 and F_2. The null and alternative hypotheses are

$$H_0 : F_1(y) = F_2(y) \quad \text{and} \quad H_A : F_1(y+\Delta) = F_2(y)$$

for all y and some constant $\Delta \neq 0$.

Because n_1 and n_2 are both ≥ 12 the large sample approximation version of the test can be used. The test statistic is

$$Z = \frac{W_1 - E(W_1)}{\sqrt{V(W_1)}}$$

where W_1 is the sum of the ranks from the Hypertension group,

$$E(W_1) = \frac{n_1(N+1)}{2}$$

and

$$V(W_1) = \frac{n_1 n_2 (N+1)}{12} - \frac{n_1 n_2}{12N(N-1)} \sum_{i=1}^{q} t_i(t_i-1)(t_i+1)$$

where $N = n_1 + n_2 = 27$, q denotes the number of sets of ties, and t_i denotes the size of the i^{th} set of ties for $i = 1, \ldots, q$. At the $\alpha = 0.05$ level of significance, the critical region is

$$C_{0.05} = \{Z : |Z| > z_{0.975} = 1.96\}.$$

To compute W_1 we first get the ranks for the observed data, assigning the midrank in the case of ties, as in the table on the next page. There are three sets of ties, each with two tied observations, so $t_i = 2$ in each case.

Here $W_1 = 238$.

Also

$$E(W_1) = \frac{15 \times 28}{2} = 210$$

and

$$V(W_1) = \frac{12 \times 15 \times 28}{12} - \frac{12 \times 15}{12 \times 27 \times 26} \cdot \sum_{i=1}^{3} (2 \times 1 \times 3) = 419.62$$

so that $Z = (238 - 210)/\sqrt{419.62} = 1.367$ and hence we do not reject the null. The p-value is $2 * \Phi(-1.367) = 0.172$. Therefore, there is insufficient evidence from these data to suggest that there is a difference in sodium intake between normal and hypertensive individuals.

Verifying the results using R:

```
> wilcox.test(hypertensive,normal,exact=F,correct=F)

        Wilcoxon rank sum test

data:  hypertensive and normal
W = 118, p-value = 0.1717
alternative hypothesis: true location shift is not equal to 0
```

Hypertensive	Rank	Normal	Rank
1100	2	1000	1
1320	5	1220	3
1350	6	1300	4
1450	8	1400	7
1600	10.5	1555	9
1850	14	1600	10.5
1900	15.5	1780	12.5
1990	17	1780	12.5
2050	19	1900	15.5
2120	20	2020	18
2200	21	2350	23
2210	22	2375	24
2500	25		
2610	26		
2720	27		

Using SAS:

```
proc npar1way wilcoxon correct=no;
 class group;
 var sodium;
```

```
         Wilcoxon Scores (Rank Sums) for Variable sodium
                   Classified by Variable group

                     Sum of    Expected      Std Dev         Mean
group           N    Scores   Under H0     Under H0        Score
-----------------------------------------------------------------
Hypertensive   15     238.0      210.0    20.484516    15.866667
Normal         12     140.0      168.0    20.484516    11.666667

                   Average scores were used for ties.


   Wilcoxon Two-Sample Test

Statistic             140.0000

Normal Approximation
Z                      -1.3669
One-Sided Pr <  Z       0.0858
Two-Sided Pr > |Z|      0.1717
```

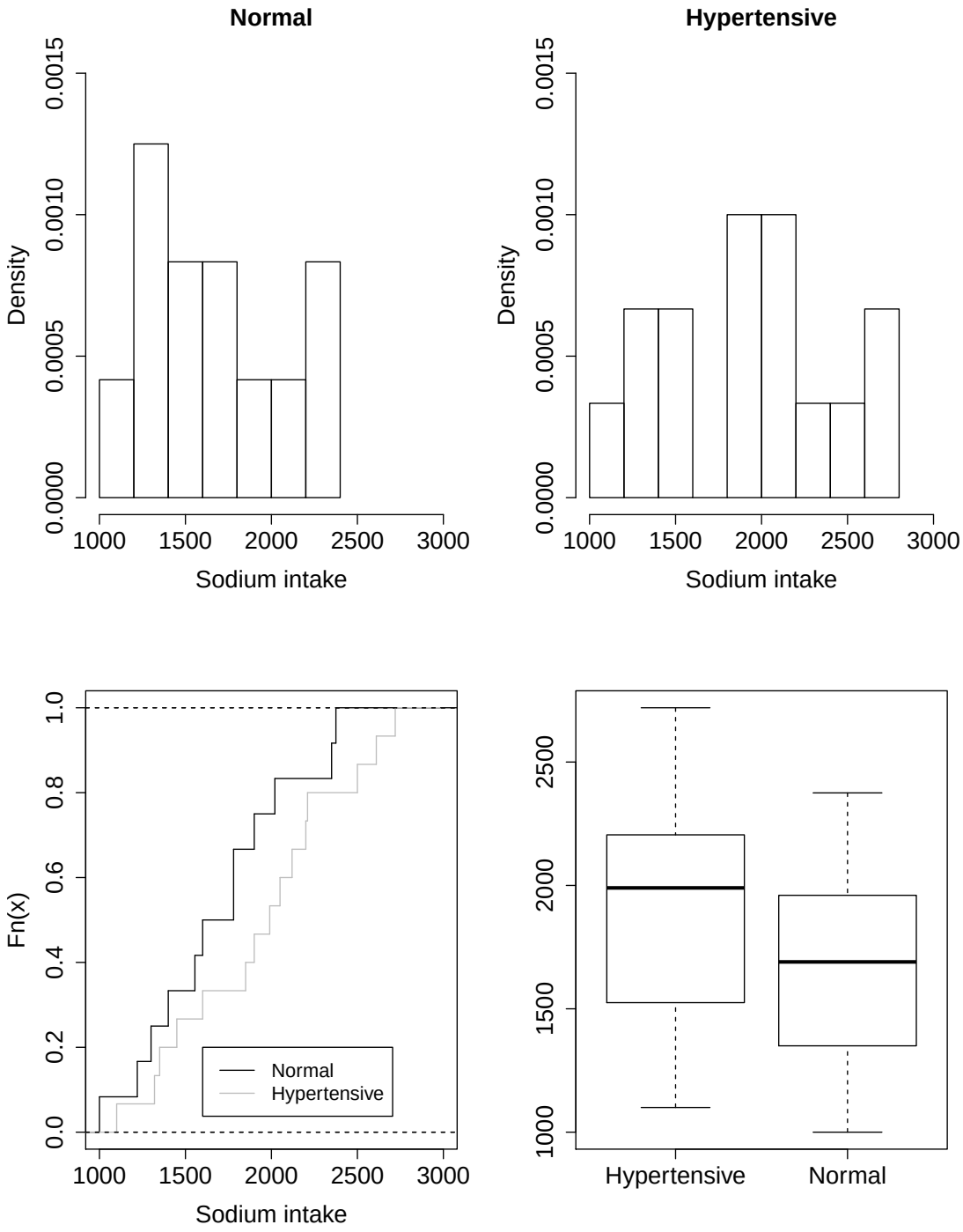

Figure 1: Histograms, EDFs, and boxplots for problem 2