Mathematical Biostatistics Boot Camp 2: Lecture 12

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Mathematical
Biostatistics
Boot Camp 2:
Lecture 12

Brian Caffo

Nonparametric
tests

Sign test

Signed rank
test

Monte Carlo

Independent
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Mann/Whitney
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Nonparametric tests

- "Distribution free" methods require fewer assumptions than parametric methods
- Focus on testing rather than estimation
- Not sensitive to outlying observations
- Especially useful for cruder data (like ranks)
- "Throws away" some of the information in the data
- May be less powerful than parametric counterparts, when the parametric assumptions are true
- For large samples, are equally efficient to parametric counterparts

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Fish	SR	P	Diff	Sgn rank	Fish	SR	P	Diff	Sng rank
1	.32	.39	.07	+15.5	13	.20	.22	.02	+6.5
2	.40	.47	.07	+15.5	14	.31	.30	-.01	-2.5
3	.11	.11	.00		15	.62	.60	-.02	-6.5
4	.47	.43	-.04	-11.0	16	.52	.53	.01	+2.5
5	.32	.42	.10	+20.0	17	.77	.85	.08	+17.5
6	.35	.30	-.05	-13.5	18	.23	.21	-.02	-6.5
7	.32	.43	.11	+20.0	19	.30	.33	.03	+9.0
8	.63	.98	.35	+23.0	20	.70	.57	-.13	-21.0
9	.50	.86	.36	+24.0	21	.41	.43	.02	+6.5
10	.60	.79	.19	+22.0	22	.53	.49	-.04	-11.0
11	.38	.33	-.05	-13.5	23	.19	.20	.01	+2.5
12	.46	.45	-.01	-2.5	24	.31	.35	.04	+11.0
					25	.48	.40	-.08	-17.5

Measurements are mecury levels in fish (ppm)

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Alternatives to the paired t-test

- Let $D_i =$ difference (P - SR)
- Let θ be the population median of the D_i
- $H_0 : \theta = 0$ versus $H_a : \theta \neq 0$ (or $>$ or $<$)
- Notice that $\theta = 0$ iff $p = P(D > 0) = .5$
- Let X be the number of times $D > 0$
  - X is then binomial(n, p)
- The sign test tests wether $H_0 : p = .5$ using X

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Example

- θ = median difference p - sr
- $H_0 : \theta = 0$ versus $H_a : \theta \neq 0$
- Number of instances where the difference is bigger than 0 is 15 out of 25 trials
- `binom.test(15, 25)`

  `p-value = 0.4244`
- Or we could have used large sample tests for a binomial proportion

  `prop.test(15, 25, p = .5)`

  `X-squared = 0.64, df = 1, p-value = 0.4237`

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Discussion

- Magnitude of the differences is discarded
  - Perhaps too much information lost
- Could easily have tested $H_0 : \theta = \theta_0$ by calculating the number of times $D > \theta_0$ and performing a binomial test
  - We can invert these tests to get a distribution free confidence interval for the median

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Signed rank test

- Wilcoxon's statistic uses the information in the **signed ranks** of the differences
- Saves some of the information regarding the magnitude of the differences
- Still tests $H_0 : \theta = 0$ versus the three alternatives
- Appropriately normalized, the test statistic follows a normal distribution
- Also the exact small sample distribution of the signed rank statistic is known (if there are no ties)

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Signed rank procedure

1. Take the paired differences
2. Take the absolute values of the differences
3. Rank these absolute values, throwing out the 0s
4. Multiply the ranks by the sign of the difference ($+1$ for a positive difference and -1 for a negative difference)
5. Cacluate the rank sum W_+ of the positive ranks

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Signed rank procedure

- If $\theta > 0$ then W_+ should be large
- If $\theta < 0$ then W_+ should be small
- Properly normalized, W_+ follows a large sample normal distribution
- For small sample sizes, W_+ has an exact distribution under the null hypothesis
- Can get critical values from tables in the textbook

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Monte Carlo

- Assume no ties
- Simulate n observations from any distribution that has $\theta = 0$ as its median
- Rank the absolute value of the data, retain the signs, calculate the signed rank statistic
- Apply this procedure over and over, the proportion of time that the observed test statistic is larger or smaller (depending on the hypothesis) is a Monte Carlo approximation to the P-value

Monte Carlo

- Here's a slightly more elegant way to simulate from the null distribution
- Consider the ranks $1, \ldots, n$
- Randomly assign the signs as binary with probability .5 of being positive and .5 of being negative
- Calculate the signed rank statistic
- Apply this procedure over and over, the proportion of time that the observed test statistic is larger or smaller (depending on the hypothesis) is a Monte Carlo approximation to the P-value

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Large sample distribution of W_+

- Under H_0 and if there are no ties
  - $E(W_+) = n(n+1)/4$
  - $Var(W_+) = n(n+1)(2n+1)/24$
  - $TS = \{W_+ - E(W_+)\}/Sd(W_+) \to \mathrm{Normal}(0,1)$
- There is a correction term necessary for ties
- Without ties, it's possible to do an exact (small sample) test

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Example

```
diff <- c(.07, .07, .00, -.04,  ...)
wilcox.test(diff, exact = FALSE)
```

- H_0 : Med diff $= 0$ vesus H_a : Med diff $\neq 0$
- $W_+ = 194.5$
- $E(W_+) = 24 \times 25/4 = 150$
- $\text{Var}(W_+) = 24 \times 25 \times 49/24 = 1,225$
- $TS = (194.5 - 150)/\sqrt{1,224} = 1.27$
- P-value $= .20$
- R's P-value (uses correction for ties) $= 0.21$

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Methods for unpaired samples

Comparing two measuring techniques A and B
Units are in deg C per gram

Method A		Method B
79.98	80.05	80.02
80.04	80.03	79.94
80.02	80.02	79.98
80.04	80.00	79.97
80.03	80.02	79.97
80.03		80.03
80.04		79.95
79.97		79.97

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The Mann/Whitney test

- Tests whether or not the two treatments have the same location
- Assumes independent identically distributed errors, not necessarily normal
- Null hypothesis can also be written more generally as a stochastic shift for two arbitrary distributions
- Test uses the sum of the ranks obtained by discarding the treatment labels
- Also called the Wilcoxon rank sum test

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The Mann-Whitney test

- Procedure
  1. Discard the treatment labels
  2. Rank the observations
  3. Calculate the sum of the ranks in the first treatment
  4. Either
     - calculate the asymptotic normal distrubtion of this statistic
     - compare with the exact distribution under the null hypothesis

Method A		Method B
7.5	21.0	11.5
19.0	15.5	1.0
11.5	11.5	7.5
19.0	9.0	4.5
15.5	11.5	4.5
15.5		15.5
19.0		2.0
4.5		4.5
180		51

Sum has to add up to $21 \times 22/2 = 231$

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Aside

Gauss supposedly came up with this in grade school

```
x =    1  +    2  +    3  +    4  + ... +    n
x =    n  +  n-1 +  n-2 +  n-3 + ... +    1
```

Therefore
```
  2x = n+1 + n+1 + n+1 + n+1 + ... + n+1
```

So 2x = n (n + 1) / 2

So x = n (n + 1) / 2

Results

- Let W be the sum of the ranks for the first treatment (A)
- Let n_A and n_B be the sample sizes
- Then
  - $E(W) = n_A(n_A + n_B + 1)/2$
  - $\mathrm{Var}(W) = n_A n_B (n_A + n_B + 1)/12$
  - $TS = \{W - E(W)\}/Sd(W) \to N(0,1)$
- Also the exact distribution of W can be calculated

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Example

- $W = 51$
- $E(W) = 8(8 + 13 + 1)/2 = 88$
- $Sd(W) = \sqrt{8 \times 13(8 + 13 + 1)/12} = 13.8$
- $TS = (51 - 88)/13.8 = -2.68$
- Two-sided P-value= .007
- R function `wilcox.test` will perform the test

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- Note that under H_0, the two groups are **exchangeable**
- Therefore, any allocation of the ranks between the two groups is equally likely
- Procedure: Take the ranks $1, \ldots, N_A + N_B$ and permute them
- Take the first N_A ranks and allocate them to Group A; allocate the remainder to Group B
- Calculate the test statistic
- Repeat this process over and over; the proportion of times the test statistic is larger or smaller (depending on the alternative) than the observed value is an exact P-value

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Notes about nonpar tests

- Tend to be more robust to outliers than parametric counterparts
- Do not require normality assumptions
- Usually have exact small-sample versions
- Are often based on ranks rather than the raw data
- Loss in power over parametric counterparts is often not bad
- Nonpar tests are not assumption free

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Permutation tests

- Permutation tests are similar to the rank-sum tests, though they use the actual data rather than the ranks
- That is, consider the null hypothesis that the distribution of the observations from each group is the same
- Then, the group labels are irrelevant
- We then discard the group levels and permute the combined data
- Split the permuted data into two groups with n_A and n_B observations (say by always treating the first n_A observations as the first group)
- Evaluate the probability of getting a statistic as large or large than the one observed
- An example statistic would be the difference in the averages between the two groups; one could also use a t-statistic

- This is an easy way to produce a null distribution for a test of equal distributions
- Similar in flavor to the bootstrap
- This procedure produces an exact test
- Less robust, but more powerful than the rank sum tests
- Very popular in genomic applications

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