# Dalla Lana School of Public Health, University of Toronto

# CHL 5225 H – Advanced Statistical Methods for Clinical Trials

# Assignment —Crossover Trials

The data for this assignment is located at:

www.andywillan.com/CHL5225H/data/CrossoverAssignment.txt
The first line of the data is: 1,82.715348081,67.856553121,1,1,1,1

The data is from a 2-sequence, 2-treatment, 2-period crossover trial comparing an active medication to placebo in patients with pain.

There are 40 patients in each sequence, and the data consists of 80 records, one for each patient.

The first column is the patient ID number.

The second column is sequence: 1 = placebo then active
2 = active then placebo

The third column is the pain score for the first period (higher scores meaning more pain).
The fourth column is the pain score for the second period.

The fifth column is a dummy indicator for break-through pain for the first period, where 1 indicates that the patient experienced break-through pain.
The sixth column is a dummy indicator for break-through pain for the second period.

The seventh column will be referred to later.

A. Through-out the assignment use one-sided tests at the level 0.05 for testing the null hypotheses of no treatment effect. That is, reject the null hypothesis of no treatment effect if (a) the one-sided p-value is less than 0.05 and (b) active is observed to be better than placebo. For the Willan procedure, use the nominal level that provides a one-sided 0.05 level test. Test of hypotheses regarding period and residual carryover should be two-sided at the level 0.05. Be sure to discuss and explain the results a little.

B. Show all intermediary steps, including the appropriate computer code and print-outs

C. E-mail your completed assignment is a single PDF file to andy@andywillan.com . NO HAND-WRITTEN MATERIAL WILL BE GRADED!!

D. The assignment is due on June 22rd 2017. Late assignments must be arranged prior to this due date.

1. Draw a bar chart showing average pain score by period and treatment. (marks: 2/25)

2. Using the pain scores to estimate the (a) treatment effect, (b) period effect and (c) bias due to residual carryover. (marks: 3/25)

3. Is the period effect statistically significant? (marks: 1/25)

4. Is the residual carryover statistically significant? (marks: 1/25)

5. Assuming that no treatment effect implies no residual carryover, use the pain scores to test the null hypothesis of no treatment effect using the Willan procedure. What is the appropriate nominal level of significance to be used for the Willan procedure? (marks: 6/25)

6. Would you arrive at the same conclusion if you used the Grizzle procedure? (marks: 2/25)

7. Again assuming that no treatment effect implies no residual carryover, use the pain scores to test the null hypothesis of no treatment effect assuming that the patients for whom missing = 1 (column 7) have missing second period data. What are the appropriate degrees of freedom for this test? What is the appropriate cut-point of the t-distribution (*i.e.* what value does the absolute value of the t-statistic have to equal or exceed before you can reject the null hypothesis at 0.05, one-sided)? For this question just ignore residual carryover (*i.e.* forget about the Willan or Grizzle procedures). (marks: 6/25)

8. Using the pain break-through data to test the null hypothesis of no treatment effect. Assume that no treatment effect implies no residual carryover. (marks: 4/25)