Stat 998, Fall 2015 (Larget)
Interferon Problem (Group Project)

Below is the statement of a former M.S. Exam problem, followed by the introduction from one of the reports. Your job is to perform a preliminary analysis of these data aimed at a class discussion.

You are to work with these randomly assigned groups.

Group	Members			
A	Colin Longhurst	Derek Norton	Shulei Wang	
B	Wentao Wuk	Jennifer Birstler	Maria Kamenetsky	
C	Chaoyang Yu	Bin Zhang	Huikun Zhang	
D	Morgan Brown	Aditya Gore	Casey Shanks	
E	Sien Deng	Kyle Hebert	Geng Li	Xinyu Song

Each group should decide on a group analytical strategy and arrive at a group solution. The groups should each prepare a **common set of key graphs** and a **common short description outlining an analytical strategy** (3 pages maximum per group). Each group will be asked to **present, using the overhead projector** its graphs and analytical strategy **in class on October 13**. Every individual person must submit via dropbox **a single page** indicating what s/he learned from the exercise, including technical points from the analysis, design considerations, or issues relating to group dynamics.

Dr. Bruce Edwards, an investigator in the Immunology Laboratory in the Wisconsin clinical Cancer Center, conducted an experiment on 8 cancer patients to test the effect of two types of Interferon (A & D) at two doses (15 and 45 units). The Interferon is administered on a specified day and a blood sample is drawn. A one week period for washout is allowed before the next dose is administered. The brand of Interferon was alternated as indicated on Table I, but the dose was given in the same order, first 15 units and then 45 units. For each blood sample drawn, a particular assay is done to measure the percent of tumor cells killed. The assays are done three times, with the killer cell (called NK cells) to target (tumor) cell ratio varied from 12.5/1 to 50/1 for the three assays.

The data from this experiment are given on Table II. Note that two pretreatment measurements are given, at Day 0 and at Day 1. Also note that some data are missing.

Dr. Edwards has three primary questions he wishes to address in this experiment:

1. Is there an Interferon effect?
2. Does the brand of Interferon matter?
3. Is there a dose effect?

Note: The tables are presented as prepared by the experimenter.

Objective: This data was collected with the intent of learning more about Interferon. Some evidence has been found to support the hypothesis that Interferon is an effective treatment against cancer, and in this particular study it is desirable to know if such a claim is supported. It is also of interest to determine whether the two brands of Interferon being tested, A and D, have the same effects, and if the dose level, 15 units versus 45 units makes a difference.

Data Collection: The experimenter in this study was Dr. Edwards of the University of Wisconsin Clinical Cancer Center. The eight subjects used in the experiment were all cancer patients in generally good condition. Each subject was injected with interferon, at weekly intervals, four times during a one month period, receiving each brand-dose combination once (see Figure 1). Both treatments involving the low dose, 15, were given before either involving the high dose. To monitor the possible effects due to these treatments, blood samples were drawn ten times during the month. On day zero a sample was drawn and no other action was taken. On day one a sample was drawn and then the interferon was administered. On day two another sample was drawn; day eight a sample, then interferon. This continued with the final interferon treatment given on day twenty-two and the final blood sample drawn on day twenty-nine. The term "day" here represents the time into the experiment for a given patient as the patients entered the experiment at different times over the course of over one year.

From the blood samples drawn at each of these ten time points, a certain number of NK (natural killer) cells were extracted. These were then mixed in a ratio of 50 NK cells to 1 target cell, where the target cells are tumor cells with chromium in them. The same mixture is also made with $2\times$ and $4\times$ as many target cells, giving ratios of 25/1 and 12.5/1. Each of these mixtures is then cooked for four hours and the goal is to see how many of the target cells are killed. This is done by measuring the amount of chromium given off by the mixture, but as some chromium would be given off spontaneously even if none of the target cells were killed, a correction is made. The portion given off because of the dead tumor cells is then expressed as a percentage of the total possible chromium that could be given off in this way. The dependent variable of interest is thus percent specific chromium release and represents a measure of how many target cells the NK cells have killed.

day	0	1	2	8	9	15	16	22	23	29
sampled	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
interferon		⇑		⇑		⇑		⇑		
dose		15		15		45		45		
patient					interferon type					
1		*D*		*A*		*D*		*A*		
2		*D*		*A*		*D*		*A*		
3		*A*		*D*		*A*		*D*		
4		*A*		*D*		*D*		*A*		
5		*A*		*D*		*A*		*D*		
6		*D*		*A*		*A*		*D*		
7		*D*		*A*		*A*		*D*		
8		*A*		*D*		*D*		*A*		

Table I. ↑ implies blood drawn; ⇑ indicates drug given.

patient	E/T	0	1	2	8	9	15	16	22	23	29
1	1	12.2	3.2	10.5	3.1	4.7	2.3	7.0	1.1	6.0	NA
1	2	15.4	5.7	17.2	8.3	6.0	4.5	18.6	0.9	10.7	NA
1	4	13.0	7.0	19.1	7.5	6.9	7.7	19.7	1.3	7.4	NA
2	1	2.3	6.1	10.0	5.0	8.3	2.5	13.5	4.7	9.4	1.1
2	2	5.6	4.9	16.1	8.6	10.7	3.7	18.6	9.9	14.5	5.5
2	4	5.2	11.5	14.7	13.9	12.1	5.2	27.6	14.2	19.7	16.3
3	1	24.9	20.0	32.5	1.4	NA	12.6	13.2	9.2	13.0	9.5
3	2	31.6	30.7	40.2	3.1	39.8	17.0	21.1	16.1	29.6	23.5
3	4	39.9	22.8	50.7	7.6	51.0	24.1	31.4	24.8	42.5	31.2
4	1	5.9	10.3	9.9	6.1	17.4	9.7	23.3	5.0	10.5	3.1
4	2	10.1	9.7	16.8	9.8	26.2	19.2	24.0	9.4	16.8	7.2
4	4	7.4	13.6	27.3	14.5	28.8	28.6	26.6	13.9	22.3	10.4
5	1	8.1	10.3	8.2	3.7	3.7	6.1	5.5	0.1	−1.3	2.0
5	2	9.1	9.7	14.0	6.2	6.5	11.3	11.6	2.0	0.8	3.2
5	4	14.4	13.6	20.0	5.4	10.8	17.5	13.8	3.7	4.8	5.7
6	1	8.8	4.5	18.8	6.5	16.6	8.6	7.0	6.0	20.3	4.3
6	2	18.6	9.4	24.6	14.1	24.9	12.1	12.3	13.8	27.7	9.0
6	4	30.1	11.8	33.9	23.4	38.2	17.1	21.5	19.1	31.4	13.6
7	1	8.8	4.4	10.5	2.7	13.0	3.6	7.9	2.6	11.6	6.0
7	2	19.6	8.9	15.0	5.8	22.6	12.7	15.6	3.8	12.1	7.0
7	4	27.9	13.2	25.1	11.8	26.5	15.9	17.2	5.7	13.1	9.8
8	1	−1.6	1.3	8.1	6.5	18.0	7.1	2.8	4.4	2.9	2.9
8	2	3.3	1.9	16.0	1.9	27.0	6.0	5.9	4.3	7.1	3.2
8	4	2.4	3.2	19.2	6.4	34.1	7.5	7.4	7.2	8.4	3.0

Table II. NK Cell Cytotoxicity (% specific ^{51}Cr release)
NA means no data available.

			Subject							
			1	2	3	4	5	6	7	8
Day 0:	Blood Drawn									
Day 1:	Blood Drawn,	then	D-15	D-15	A-15	A-15	A-15	D-15	D-15	A-15
Day 2:	Blood Drawn									
Day 8:	Blood Drawn	then	A-15	A-15	D-15	D-15	D-15	A-15	A-15	D-15
Day 9:	Blood Drawn									
Day 15:	Blood Drawn	then	D-45	D-45	A-45	D-45	A-45	A-45	A-45	D-45
Day 16:	Blood Drawn									
Day 22:	Blood Drawn	then	A-45	A-45	D-45	A-45	D-45	D-45	D-45	A-45
Day 23:	Blood Drawn									
Day 29:	Blood Drawn									

Figure 1. Schematic showing design of experiment. Brand of Interferon is given by (A,D) and dose by (15,45).