Lecture 31

Analysis of Covariance

STAT 512

Spring 2011

Background Reading

KNNL: Chapter 22

Topic Overview

- Covariates; a couple of extreme examples
- ANCOVA
- “Adjusted” or Least-Squares Means

Analysis of Covariance

- ANCOVA is really "ANOVA with covariates" or, more simply, a combination of ANOVA and regression

- Use when you have some categorical factors and some quantitative predictors. Continuous variables are referred to as ***covariates*** or ***concomitant variables***.

Analysis of Covariance (2)

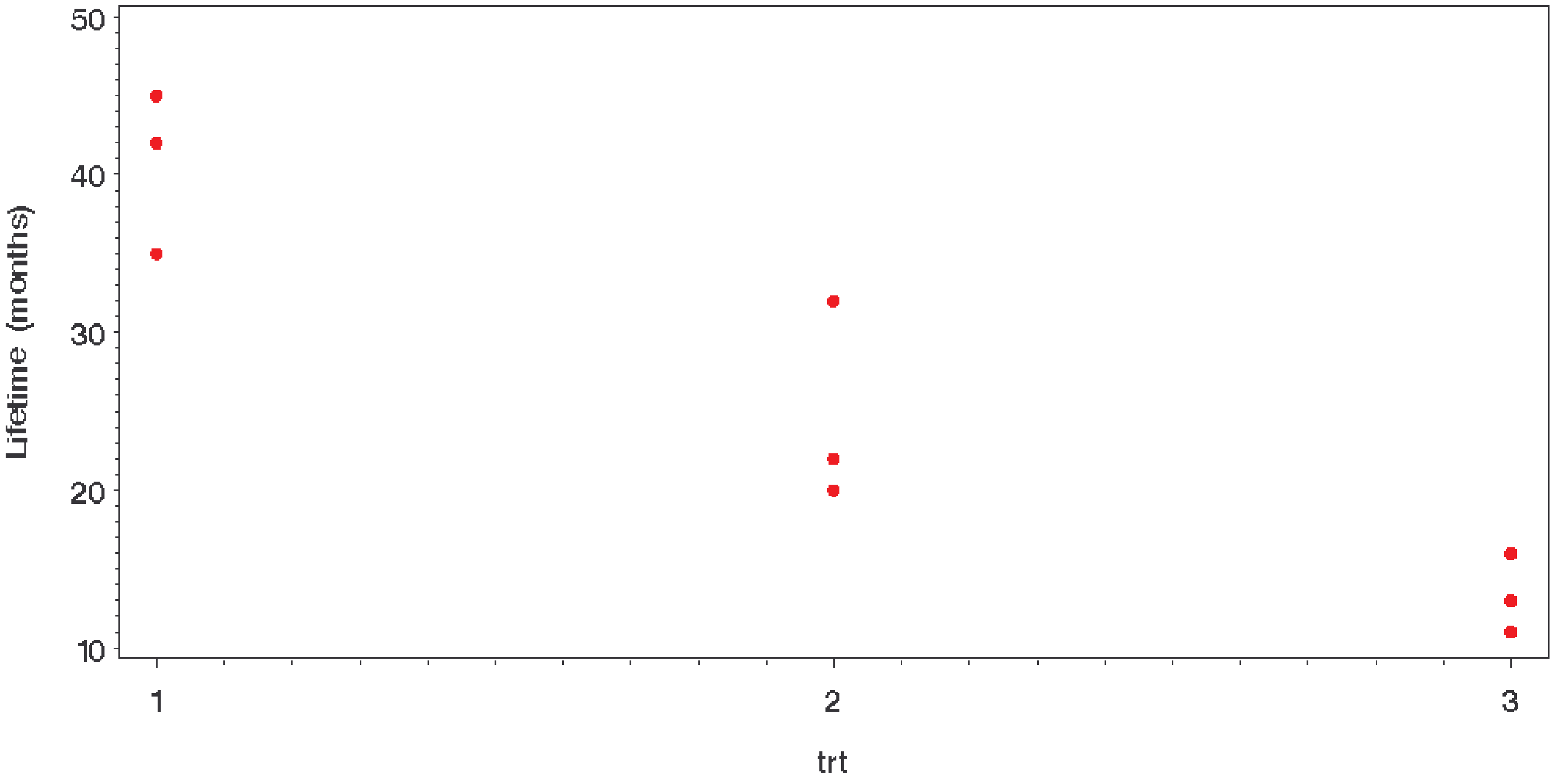
- Similar to ***blocking*** - the idea is that concomitant variables are not necessarily of primary interest, but still their inclusion in the model will help explain more of the response, and hence reduce the error variance.

- In some situations, failure to include an important covariate can yield misleading results.

Example #1

- Studying three potential treatments of an aggressive form of cancer.
- Response variable is the number of months a patient lives after being placed on a treatment.
- We will analyze the data as a one-way ANOVA (see ancova.sas for code).

Plot of the data against TRT



ANOVA Results

```
                          Sum of
Source          DF       Squares     Mean Square    F Value    Pr > F
TRT              2   1131.555556      565.777778      22.94    0.0015
Error            6    148.000000       24.666667
Total            8   1279.555556
```

- Seems clear there is a significant treatment effect, right?

```
             y LSMEAN   trt     Number
A      40.66667     1            1

B      24.66667     2            2
B
B      13.33333     3            3
```

ANOVA Results (2)

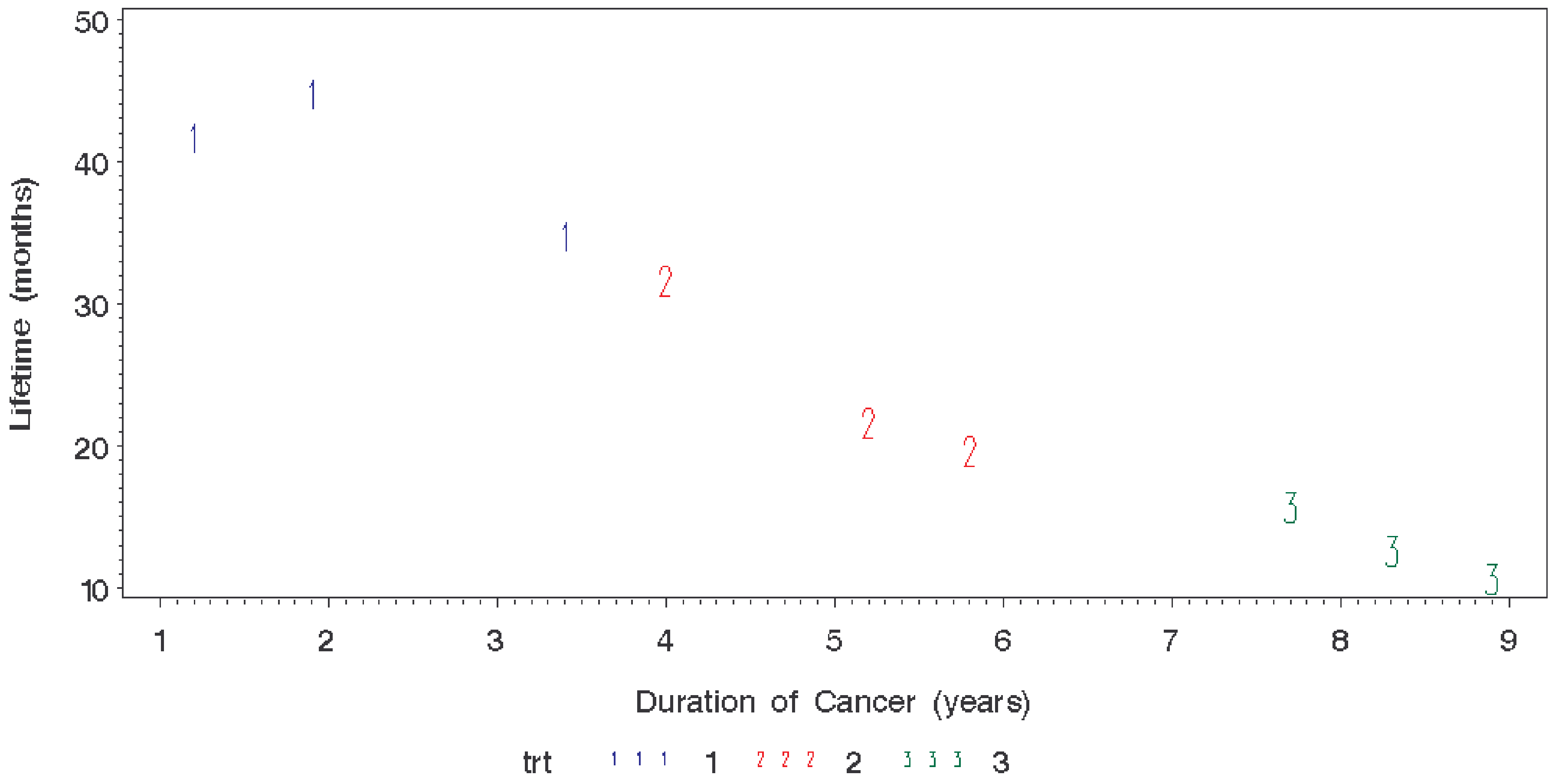
- The analysis tells us that there is a significant treatment effect. It suggests that Treatment 1 is clearly the best (since people live longer).

- So we put a large group of people on Treatment 1 expecting them to live 40+ months, but unfortunately they do not live this long. What did we do wrong????

The oversight...

- Consider the stage to which the cancer has progressed at the time that treatment begins.
- This is important, because those at earlier stages of disease will naturally live longer on average.
- The following plot illustrates where things went awry:

Plot of Y vs X by TRT



Lifetime vs Duration

- There is clearly a linear relationship between the duration of the cancer and the length of time someone has left to live.
- Furthermore, we notice from the plot that the group assigned to the first treatment were all in an earlier stage of the disease, those assigned to the second treatment were all in a middle stage, and those assigned to the third treatment were all in a later stage.

Treatment Effects?

- After seeing this plot, it is clear that we can’t compare the lifetimes without considering the duration of the disease.
- We would suspect looking at this plot to find the treatments are not all that different. The following ANCOVA output leads to that conclusion:

```
Source     DF              SS      Mean Square    F Value     Pr > F
  x        1      1225.166536      1225.166536     199.15     <.0001
  trt      2        23.628758        11.814379       1.92     0.2405
  Error    5        30.760262         6.152052
  Total    8      1279.555556
```

MEANS vs. LSMEANS

- The MEANS statement compares the unadjusted means – for this problem that is WRONG. This was the original output we considered, where Treatment 1 appeared to be the best.
- The LSMEANS statement adjusts for any concomitant variables in the model. You can think of the LSMEAN for a given treatment as the "mean response for that treatment, at the AVERAGE value(s) of the covariate(s)"

MEANS vs. LSMeans (2)

trt	N	Mean	LSMEAN	LSMEAN #
1	3	40.67	26.09	1
2	3	24.67	23.91	2
3	3	13.33	28.67	3

```
          y LSMEAN   trt      Number
A       28.67261     3             3
A
A       26.08623     1             1
A
A       23.90783     2             2
```

MEANS vs. LSMeans (3)

- Using MEANS, not only would we find significant differences that are not really there, but...

- LSMeans indicate that, if there exists a “best” treatment, it would be Treatment 3, *not Treatment 1*. So using the incorrect analysis to make decisions could be a deadly mistake.

Conclusions

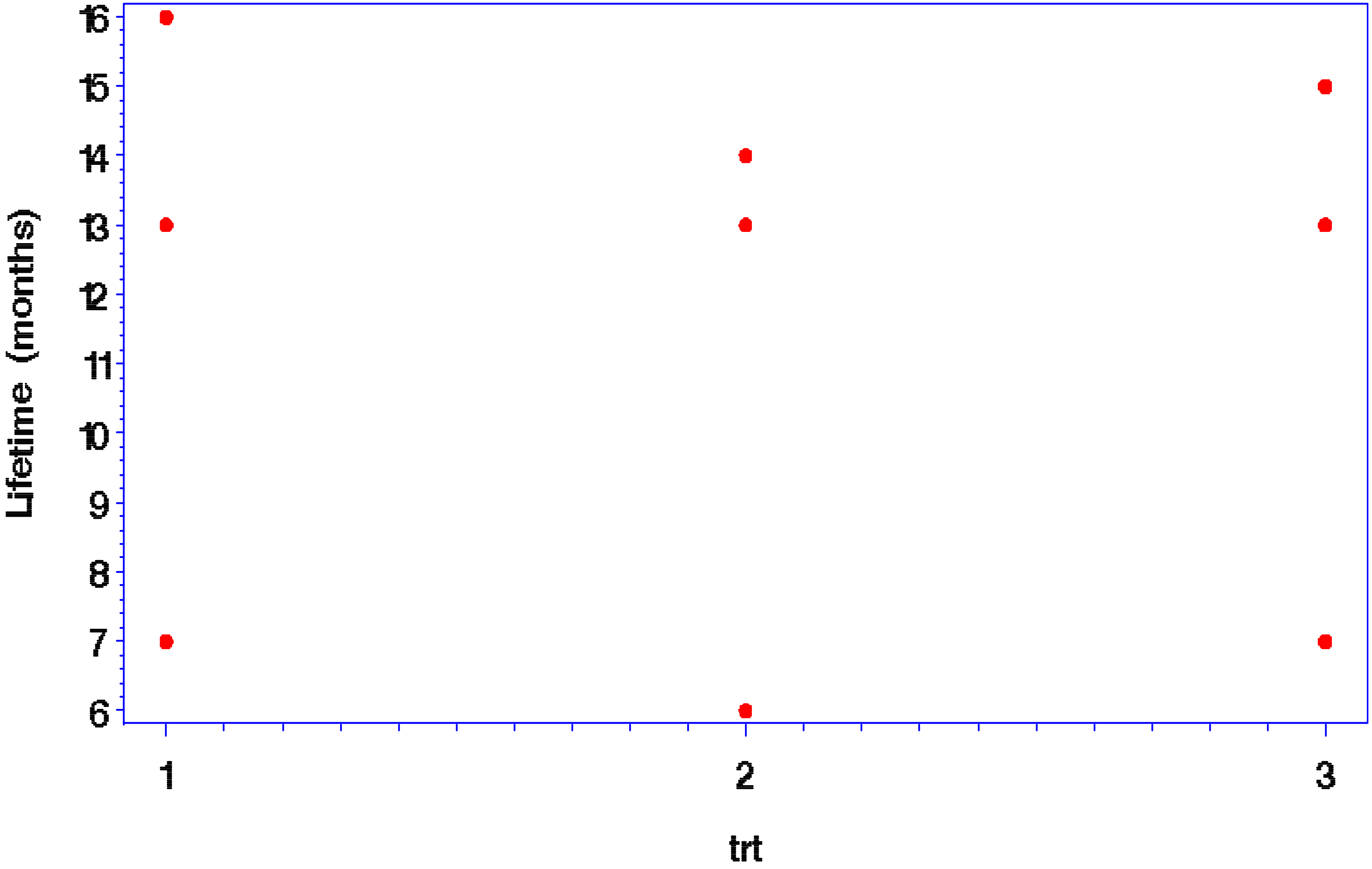
- Stage of disease is the contributing factor toward lifetime – it really didn’t have anything to do with the choice of treatment.
- It just happened that everyone on treatment 1 was in an earlier stage of the disease and so that made it look like there was a treatment effect. In fact, if we were to recommend a treatment, we might prefer Treatment #3 (although there is no sig. difference among any of the treatments).

A Second Example

- It is also possible to have a difference in means, but not be able to see it unless you first adjust for a covariate.

- Consider the same type of setting as where we want to test the effect of treatment on cancer, but with different data.

Plot of Y vs TRT

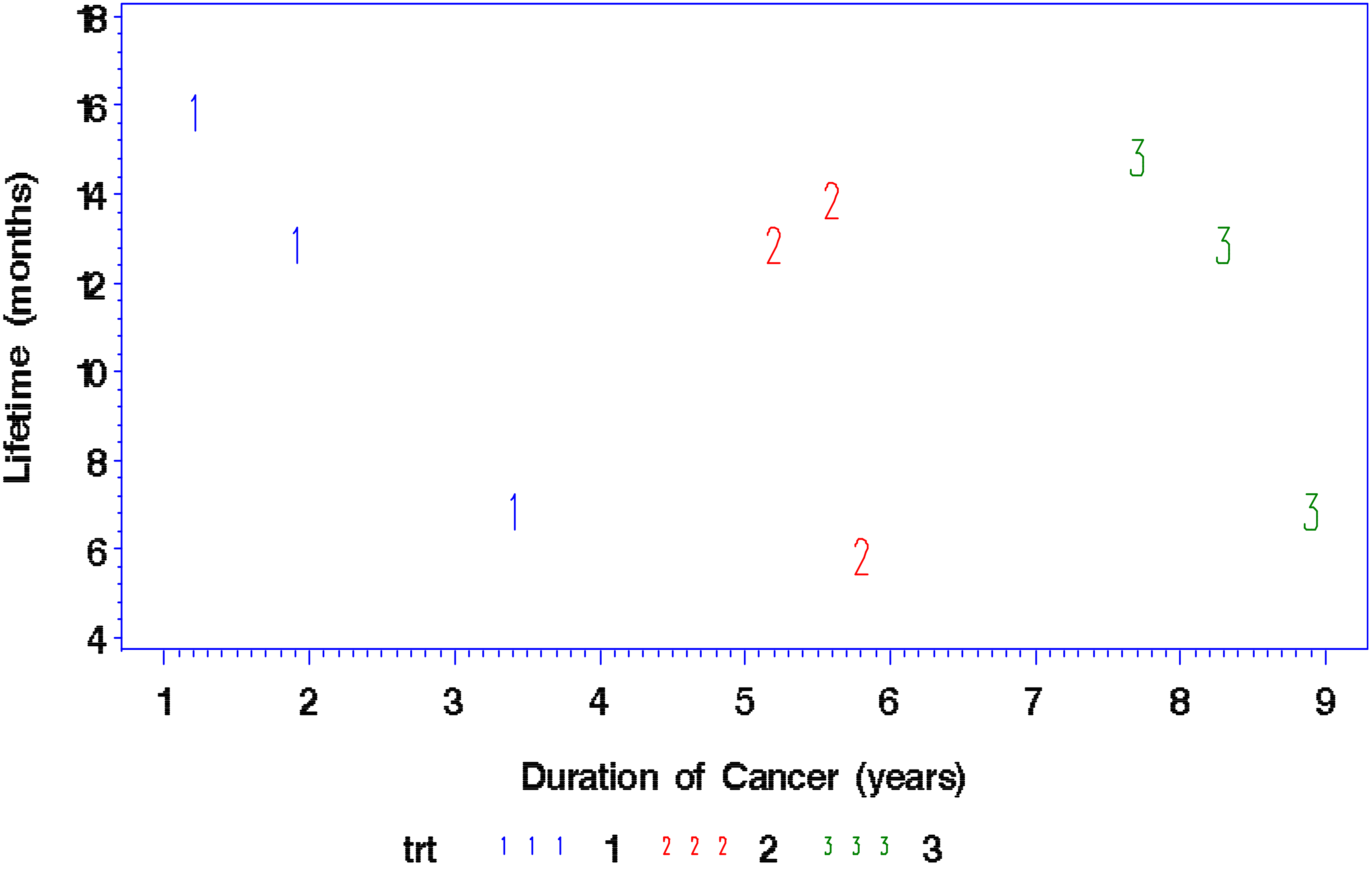


ANOVA Results

```
Source  DF    SS     MS       F    Pr > F
TRT      2    1.56   0.78   0.04   0.9604
Error    6  114.67  19.11
Total    8  116.22
```

- No significant differences between the treatments, right? WRONG! Consider now what happens when we again consider the covariate (stage of disease):

Plot of Y vs X by TRT



Covariate

- Again all taking Treatment 1 were in the early stages of the disease, all on Treatment 2 in the middle stages, and all on Treatment 3 in the latter stages.
- Is there a treatment effect? Treatment 3 appears to be keeping those at advanced stages of disease alive equally as long as Treatment 1 does for those in early stages. Surely Treatment 3 is better.

ANCOVA

```
Source  DF      SS      MS  F Value  Pr > F
Time     1    6.98    6.98   1.11    0.3407
trt      2   77.77   38.88   6.18    0.0446
Error    5   31.48    6.30
Total    8  116.22
```

- Note that duration of the cancer by itself appears insignificant (if we look at Type I SS).

ANCOVA (2)

- We must realize that the duration of the cancer at time of treatment IS important and MUST be included in the model – or we get mistaken results. We must adjust for it before we can see the differences in treatments.

- Note: the duration actually will test as important, but we cannot see it here until the treatments are in the model (see Type III sums of squares).

LSMEANS

```
          y LSMEAN     trt     Number
A        26.269579     3            3

B        11.984466     2            2
B
B        -3.587379     1            1
```

Conclusions

- The output indicates that Treatment #3 is significantly better than the other two treatments.
- This time the potentially deadly mistake would be to assume based on a one-way ANOVA that the treatments were equivalent and use the cheapest one (unless you were lucky and that was Treatment #3)
- Note that these examples were just for illustration – in reality, one should redesign this experiment and collect more data.

Data for one-way ANCOVA

- Y_{ij} is the j^{th} observation on the response variable in the i^{th} group

- X_{ij} is the j^{th} observation on the covariate in the i^{th} group

- $i = 1, \ldots, r$ levels (groups) of factor

- $j = 1, \ldots, n_i$ observations for level i

Basic ideas behind ANCOVA

- Covariates (concomitant variables) can reduce the MSE, thereby increasing power for testing. And as we have seen, sometimes they are absolutely necessary in order to get accurate analysis.
- A covariate can adjust for differences in characteristics of subjects in the treatment groups. Baseline or pretest values are often used as covariates.

Assumptions

- Ideally the covariate will not be in any way related to the treatment variables (factors).

- We assume that the covariate will be linearly related to the response and that the relationship will be the same for all levels of the factor (no interaction between covariate and factor).

Cell Means Model

$$Y_{ij} = \mu_i + \beta\left(X_{ij} - \bar{X}_{\bullet\bullet}\right) + \varepsilon_{ij}$$

- As usual $\varepsilon_{ij} \overset{iid}{\sim} N\left(0, \sigma^2\right)$
- $Y_{ij} \sim N\left(\mu_i + \beta\left(X_{ij} - \bar{X}_{\bullet\bullet}\right), \sigma^2\right)$, independent
- For each *i*, we have a simple linear regression in which <u>the slopes are the same</u>, but the intercepts may differ (i.e. different means once covariate has been "adjusted" out).

Parameters

- The parameters of the model are $\mu_1, \mu_2, \ldots, \mu_r, \beta, \sigma^2$.

- We use multiple regression methods to estimate the μ_i and β

- We use the residuals from the model to estimate σ^2 (via the MSE)

Factor Effects Model

$$Y_{ij} = \mu + \alpha_i + \beta\left(X_{ij} - \bar{X}_{\bullet\bullet}\right) + \varepsilon_{ij}$$

- Again, $\varepsilon_{ij} \overset{iid}{\sim} N\left(0, \sigma^2\right)$
- Constraints: $\sum \alpha_i = 0$ (or in SAS $\alpha_a = 0$)
- Expected value of a Y with level i and $X_{ij} = x$ is $\mu + \alpha_i + \beta\left(x - \bar{X}_{\bullet\bullet}\right)$
- Note: the difference $\alpha_i - \alpha_{i'}$ does NOT dependent on the value of *x*.

LSMeans

- LSMEAN for treatment *i* is the expected value of a Y with level i and $X_{ij} = \overline{x}_{\cdot\cdot}$

- Value of LSMEAN for treatment *i* is $\mu + \alpha_i + \beta\overline{x}_{\cdot\cdot}$

- Also known as the *adjusted estimated treatment mean*.

SAS LSMeans Statement

- STDERR gets the standard errors for the least-square means
- TDIFF requests the matrix of statistics (with p-values) that will do pairwise comps. PDIFF gets the p-values
- For multiple comparison procedures, add ADJUST=<type> where <type> can be TUKEY, BON, SCHEFFE, DUNNETT
- CL gets confidence limits for the means (and differences in conjunction with PDIFF).

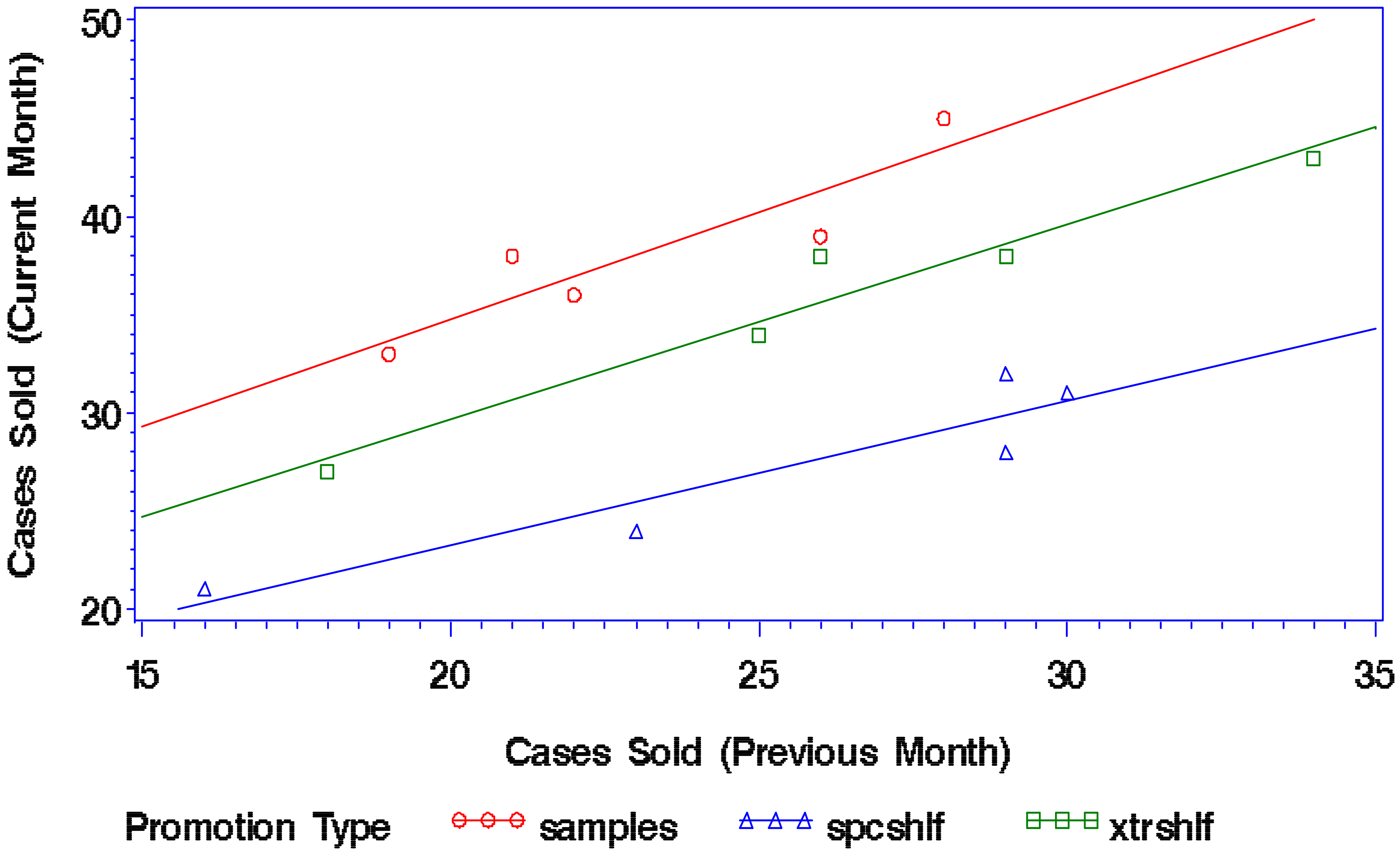
Crackers Example

(crackers.sas)

- Y is then number of cases of crackers sold during promotion period
- Factor is the type of promotion (r=3)
  - 1 = customers sample in store
  - 2 = added shelf space
  - 3 = special display cells
- n_i = 5 different stores per type
- The *covariate* X is the number of cases of crackers sold in the preceding period.

Plot of the Data

With Regression Lines



Analysis in SAS

```
proc glm data=a1;
   class promo;
   model cases=last promo
                 /solution clparm;
   lsmeans promo /adjust=tukey stderr
                  tdiff pdiff cl;
run;
```

Reminder: Check assumptions!

Output

```
Source  DF     SS      MS      F     Pr > F
last     1   190.68  190.68  54.38   <.0001
promo    2   417.15  208.58  59.48   <.0001
Error   11    38.57    3.51
Total   14   646.40

R-Square     0.940329

Source  DF   SS-III    MS   F Value   Pr > F
last     1   269.03  269.03  76.72    <.0001
promo    2   417.15  208.58  59.48    <.0001
```

```
Parameter              EST          SE    T-value
Intercept            12.28 B      2.83      4.33
last                  0.90        0.10      8.76
promo    samples      5.08 B      1.23      4.13
promo    spcshlf     -7.90 B      1.19     -6.65
promo    xtrshlf      0.00 B       .         .

Parameter              Pr > |t|         95% CL
Intercept               0.0012        6.04   18.52
last                    <.0001        0.67    1.12
promo    samples        0.0017        2.37    7.78
promo    spcshlf        <.0001      -10.52   -5.29
promo    xtrshlf          .             .       .
promo       LSMEAN    SE     Pr > |t| LSMEAN#
samples     39.82   0.858    <.0001      1
spcshlf     26.84   0.838    <.0001      2
xtrshlf     34.74   0.850    <.0001      3

i/j           1             2            3
 1                       <.0001       0.0044
 2         <.0001                     <.0001
 3         0.0044        <.0001

promo       LSMEAN    95% Confidence Limits
samples      39.82        37.93    41.70
spcshlf      26.84        25.00    28.69
xtrshlf      34.74        32.87    36.61
```

Conclusions

- Providing Samples is the most effective sales tactic (significantly better than the other two)
- Extra shelf space devoted to an item is more effective than a special display

Conclusions (2)

- Common slope is 0.9. The option ‘clparm’ can be used to get confidence intervals on the parameters. Note however that only CI’s for UNBIASED estimates (in this case the slope for LAST) are appropriate. The 95% CI for the slope was found to be (0.67,1.12).
- Note: Might have done this analysis by analyzing the difference in cases sold (single factor ANOVA)

Upcoming in Lecture 32...

- Two-way Analysis of Covariance
- More Examples