

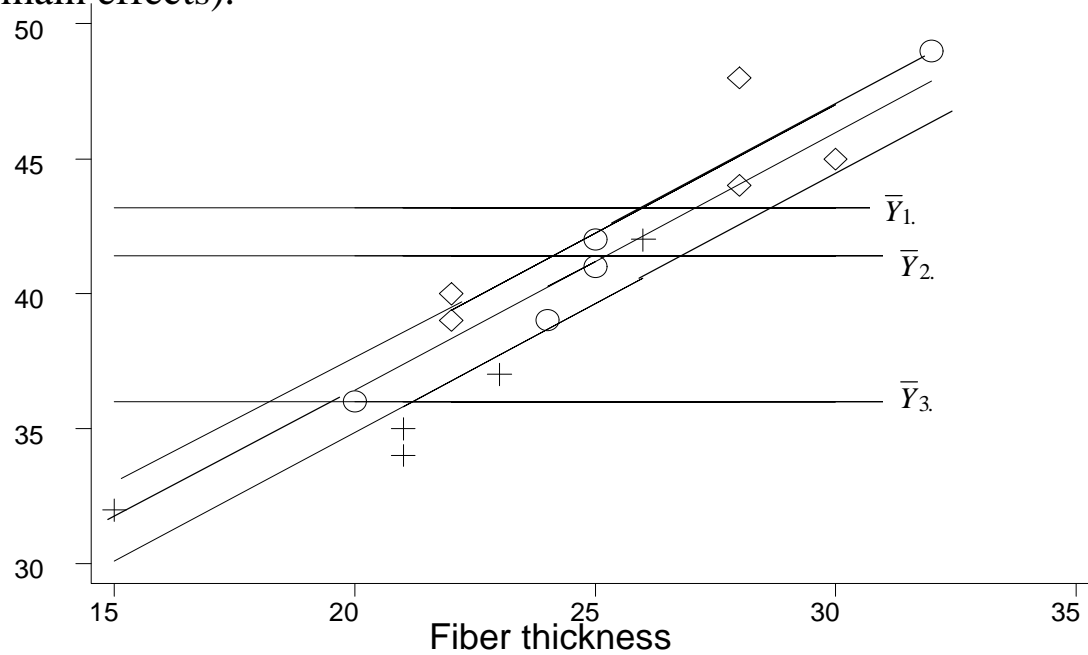
### **The analysis of covariance (ANACOVA)**

The analysis of covariance is an extension of the analysis of variance technique. Like ANOVA, several factors may be compared but in addition, all the observations are “adjusted” by (regressed on) a number of continuous variables.

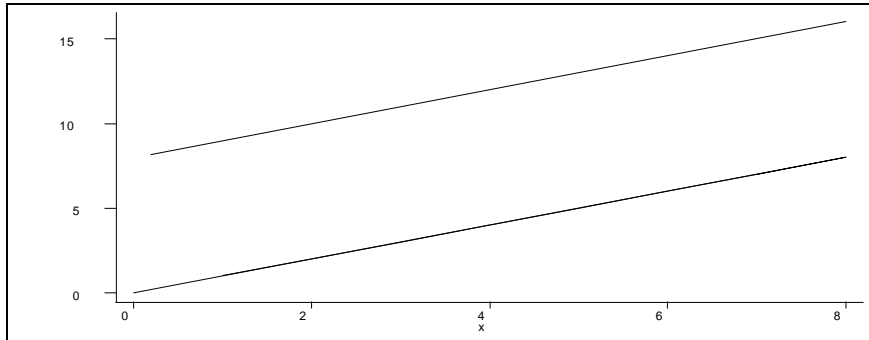
The simplest analysis of covariance model involves one nominal (categorical) and one continuous variable (covariate, or concomitant variable) and equal number of observations per cell as follows:

That is, there is a part of the model that is exactly like a (one-way) analysis of variance, and then there is an adjustment for the relationship of  $y$  on  $x$ .

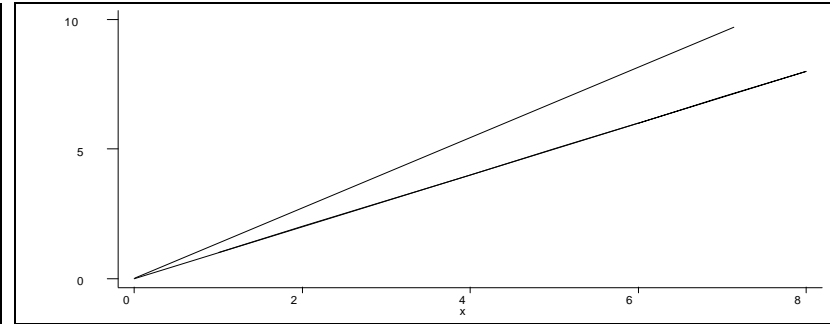
For example, consider the following figure from an industrial experiment. There are three machines that test the strength of a fiber. Strength is also associated however, with the thickness (or diameter) of the fiber. Notice how the deviations from the regression lines are dramatically reduced compared to those from the mean (horizontal) lines that correspond to a one-way analysis of variance among the three machines (main effects).



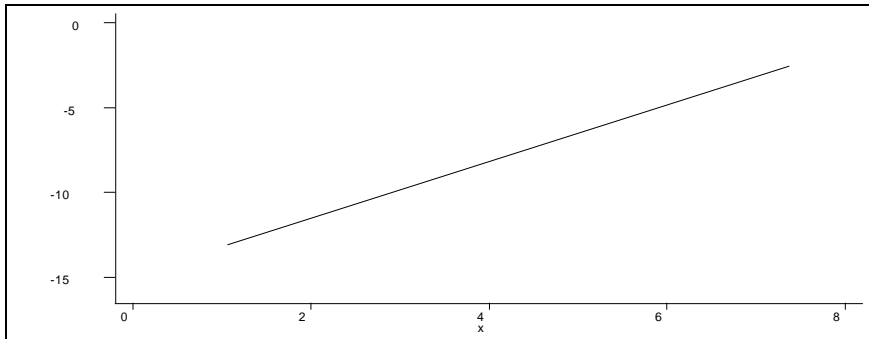
I



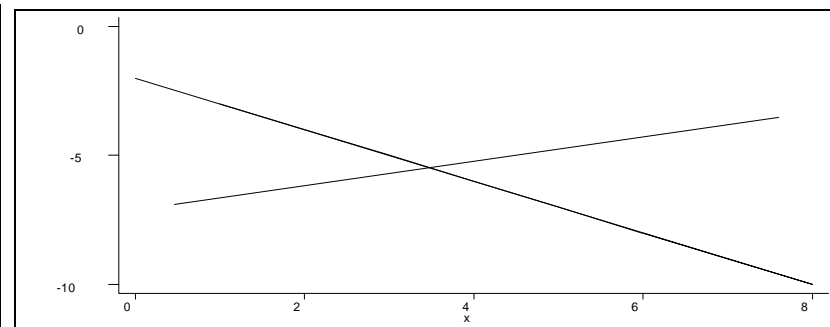
II



III



IV



**I. Parallel lines.** In this case, intercepts  $\beta_{10} \neq \beta_{20}$ , but the slopes are equal; i.e.,  $\beta_{11} = \beta_{21}$

**II. Non-parallel lines.** In II,  $\beta_{10} = \beta_{20}$  but  $\beta_{11} \neq \beta_{21}$

**III. Coincident lines.** In this case, both  $\beta_{10} = \beta_{20}$  and  $\beta_{11} = \beta_{21}$ .

**IV. Non-parallel lines.** Both the intercept and slope are different

### **Relevant scientific questions in the analysis of covariance**

Frequently asked questions in the analysis of covariance are usually expressed as follows:

1. *Parallelism.* This question has to do with whether the relationship between the dependent variable and the covariate is the same in all groups considered (cases I and III above). If this is not the case, then we say that there is *interaction* between the groups and the covariate (see cases II and IV above).
2. *Differences among groups.* Usually the covariate is of secondary importance. Its primary use is as a necessary adjustment, in order to increase the precision of inference. The primary question is whether the mean values of the dependent variable in all groups are equal *after adjustment for the covariate.*

**Comments:**

1. In cases **I** and **III** the slopes are equal, which means that the relationship between the dependent variable and the covariate is identical in both groups. Parallelism implies that the difference between groups is constant and is equal to the differences in the intercepts. Thus, the statistical test that investigates differences among the groups is based on the differences of the group intercepts
2. In cases **II** and **IV**, the slopes are not equal, that is interaction is present, then the relationship between the dependent variable and the covariate is different in each group. Thus, we are no longer able to talk about adjustment for the covariate and separate analyses should be carried out. The conclusions from the statistical analysis must now focus on the different relationships between the dependent variable and covariate in the two groups rather than the difference in the adjusted mean values of the dependent variable in the groups. Thus, in that case, we will have several regression analyses rather than an analysis of variance of adjusted mean group values.

### Definitions

To understand what happens by the adjustment with the continuous covariate we define the following quantities:

$$1. S_{yy} = \sum_{i=1}^a \sum_{j=1}^n (y_{ij} - \bar{y}_{..})^2, S_{xx} = \sum_{i=1}^a \sum_{j=1}^n (x_{ij} - \bar{x}_{..})^2, S_{xy} = \sum_{i=1}^a \sum_{j=1}^n (x_{ij} - \bar{x}_{..})(y_{ij} - \bar{y}_{..})$$

$$2. T_{yy} = \sum_{i=1}^a \sum_{j=1}^n (\bar{y}_{i.} - \bar{y}_{..})^2, T_{xx} = \sum_{i=1}^a \sum_{j=1}^n (\bar{x}_{i.} - \bar{x}_{..})^2, T_{xy} = \sum_{i=1}^a \sum_{j=1}^n (\bar{x}_{i.} - \bar{x}_{..})(\bar{y}_{i.} - \bar{y}_{..})$$

$$3. E_{yy} = \sum_{i=1}^a \sum_{j=1}^n (y_{ij} - \bar{y}_{i.})^2 = S_{yy} - T_{yy}, E_{xx} = \sum_{i=1}^a \sum_{j=1}^n (x_{ij} - \bar{x}_{i.})^2 = S_{xx} - T_{xx}$$

$$E_{xy} = \sum_{i=1}^a \sum_{j=1}^n (x_{ij} - \bar{x}_{i.})(y_{ij} - \bar{y}_{i.}) = S_{xy} - T_{xy}$$

In general, the prefixes  $S$ ,  $T$  and  $E$  refer to sums of squares and cross-product terms for total, treatments and error respectively, and usually,  $S=T+E$ .

### ANACOVA as an “adjusted” ANOVA

Recall that in the absence of treatment groups or, equivalently, in the absence of a statistically

significant treatment effect, the least squares estimate of  $\beta$  is  $\hat{\beta} = \frac{\sum_{i=1}^a \sum_{j=1}^n (x_{ij} - \bar{x}_{..})(y_{ij} - \bar{y}_{..})}{\sum_{i=1}^a \sum_{j=1}^n (x_{ij} - \bar{x}_{..})^2} = \frac{S_{xy}}{S_{xx}}$ .

Also, the unadjusted (for the treatments) regression sum of squares is  $SSR' = \left(S_{xy}\right)^2 / S_{xx}$ , while

$SSE' = S_{yy} - \left(S_{xy}\right)^2 / S_{xx}$  with 1 and  $a(n-1)-1$  degrees of freedom respectively.

### ANACOVA as an “adjusted” ANOVA (continued)

On the other hand, if treatment groups do exist, or, equivalently, there is a significant treatment effect, then the least squares estimate of  $\beta$  is a weighted average of the least squares estimates of  $b$  in each treatment group

$$\hat{\beta} = \frac{\sum_{j=1}^n (x_{1j} - \bar{x}_{1.})^2 \hat{\beta}_1 + \sum_{j=1}^n (x_{2j} - \bar{x}_{2.})^2 \hat{\beta}_2 + \cdots + \sum_{j=1}^n (x_{aj} - \bar{x}_{a.})^2 \hat{\beta}_a}{\sum_{j=1}^n (x_{1j} - \bar{x}_{1.})^2 + \sum_{j=1}^n (x_{2j} - \bar{x}_{2.})^2 + \cdots + \sum_{j=1}^n (x_{aj} - \bar{x}_{a.})^2} = \frac{E_{xy}}{E_{xx}} = \frac{S_{xy} - T_{xy}}{S_{xx} - T_{xx}}$$

By similar arguments as in the case of simple linear regression, it can be shown, that the sum of squares for the regression adjusted for the treatment effect is  $SSR = (E_{xy})^2 / E_{xx}$ , while the residual sum of squares is  $SSE = E_{yy} - (E_{xy})^2 / E_{xx} = (S_{yy} - T_{yy}) - (E_{xy})^2 / E_{xx} = SSY - SST - SSR$ , where  $SST$  is the usual treatment sum of squares.



<b>Analysis of Covariance table</b>					
<b>(expressed as an adjusted analysis of variance)</b>					
Source of variability	Sums of squares (SS)	Df	Mean squares (MS)	F	Prob > F
Regression	$SSR = (S_{xy})^2 / S_{xx}$	1	$MSR = SSR$	$F = \frac{MSR}{MSE}$	
Treatments	$SSE' - SSE = S_{yy} - (S_{xy})^2 / S_{xx} - [E_{yy} - (E_{xy})^2 / E_{xx}]$	$a-1$	$MST = \frac{SSE' - SSE}{a-1}$	$F = \frac{MST}{MSE}$	$p = P(F > F_{a-1, a(n-1)-1; p})$
Error	$SSE = E_{yy} - (E_{xy})^2 / E_{xx}$	$a(n-1)-1$	$MSE = \frac{SSE}{a(n-1)-1}$		
<b>Total</b>	$S_{yy}$	$an-1$			

**Comments.**

1. The error sum of squares  $SSE' > SSE$  since the latter results from the addition of the treatment effect. The  $F$  test is based on  $F = \frac{(SSE' - SSE) / (a - 1)}{SSE / [a(n - 1) - 1]} \sim F_{a - 1, a(n - 1) - 1}$  is a partial  $F$  test that investigates the statistical significance of adding the treatment effect after the regression model.
2. The  $F$  test involving  $MSR$ ,  $F = \frac{(MSR)}{SSE' / [a(n - 1) - 1]} \sim F_{1, a(n - 1) - 1}$  merely tests whether there is a statistically significant relationship between the covariate and the dependent variable. This is not an appropriate test for testing parallelism between the lines corresponding to the treatment groups.
- 3.

**ANACOVA for a single-factor experiment with one covariate**

In this simplest case, both the significance of the regression (adjusted for the effect of treatment) and the treatment effect (adjusted for the covariate) are important. The ANACOVA table in this case is as follows:

Source of Variability	Sums of squares (SS)	Df	Mean squares (MS)	F	Prob > F
Regression	$SSR = (E_{xy})^2 / E_{xx}$	1	$MSR = SSR$	$F = \frac{MSR}{MSE}$	$p = P(F > F_{1, a(n-1)-1; p})$
Treatments	$SSE' - SSE = S_{yy} - (S_{xy})^2 / S_{xx} - [E_{yy} - (E_{xy})^2 / E_{xx}]$	$a-1$	$MST = \frac{SSE' - SSE}{a-1}$	$F = \frac{MST}{MSE}$	$p = P(F > F_{a-1, a(n-1)-1; p})$
Error	$SSE = E_{yy} - (E_{xy})^2 / E_{xx}$	$a(n-1)-1$	$MSE = \frac{SSE}{a(n-1)-1}$		
<b>Total</b>	$S_{yy}$	$an-1$			

1. Test for the significance of regression To assess the significance of regression, the hypotheses tests that are constructed are as follows:

a.  $H_0: \beta=0$

The alternative hypotheses are constructed as follows:

i.  $H_a: \beta \neq 0$  (two-sided tests)    ii.  $\left. \begin{array}{l} H_a: \beta > 0 \\ H_a: \beta < 0 \end{array} \right\}$  (one - sided tests)

b. The test statistic is  $F = \frac{MSR}{MSE} = \frac{(E_{xy})^2 / E_{xx}}{[E_{yy} - (E_{xy})^2 / E_{xx}] / [a(n-1) - 1]} \sim F_{1, a(n-1) - 1}$ . This a Type III

partial  $F$  test of the regression in the presence of treatments and is equivalent to the  $t$  test based on

the statistic  $T = \frac{\hat{\beta}}{\text{s.e.}(\hat{\beta})} \sim t_{a(n-1) - 1}$ .

c. The null hypothesis of non-significant regression is rejected if  $F > F_{1, a(n-1) - 1; 1 - \alpha}$  which is equivalent to rejecting the null hypothesis in favor of the two-sided alternative with  $|T| > t_{a(n-1) - 1; 1 - \alpha/2}$ .

On the other hand, the null hypothesis is rejected in favor of the one-sided alternative hypotheses, if

$T > t_{a(n-1) - 1; 1 - \alpha}$  and  $T < t_{-a(n-1) - 1; \alpha}$  respectively.

2. Test of parallelism In order to test for parallelism, the following model is assumed:

$$y_{ij} = \mu + \tau_i + \beta(x_{ij} - \bar{x}_{..}) + \gamma_i(x_{ij} - \bar{x}_{..}) + \epsilon_{ij} \begin{cases} i = 1, 2, \dots, a \\ j = 1, 2, \dots, n \end{cases}$$

The slope for the  $i^{\text{th}}$  treatment is given by  $\beta^* = \beta + \gamma_i$ . The term  $\gamma_i$  is called the *interaction* term.

Just like the main (categorical) effect, a usual assumption is that  $\sum_{i=1}^a \gamma_i = 0$ . The test for parallelism is constructed as follows:

a.  $H_0: \gamma_1 = \gamma_2 = \dots = \gamma_a = 0$  versus  $H_a$ : at least some of the  $\gamma$ 's are not zero.

b. The test statistic  $F = \frac{[\text{SSR}(X, Z, XZ) - \text{SSR}(X, Z)] / (a - 1)}{\text{MSE}(X, Z, XZ)} \sim F_{a-1, a(n-1) - (a-1) - 1}$  defines a Type III

partial  $F$  test, where  $\text{SSR}(X, Z, XZ)$  is the regression sum of squares of the full model that includes the interaction term, while  $\text{SSR}(X, Z)$  is the model with only treatment and regression effects and no interaction, and  $\text{MSE}(X, Z, XZ)$  is the mean square error from the full model.

c. The null hypothesis (of no interaction, or of parallel lines across treatment groups) is rejected

if  $F > F_{a-1, a(n-1) - (a-1) - 1; \alpha}$

### 3. Test of no difference in the slopes

If the test for no-interaction (parallelism) is rejected, we can consider the regression lines as parallel.

Geometrically, parallel lines have a constant distance between them that corresponds to the difference between their slopes. In the model above, the difference of slopes  $i$  and  $j$  amounts to comparison of treatment  $\tau_i$  versus  $\tau_j$ , i.e.,  $\beta_{oi} - \beta_{oj} = \tau_i - \tau_j$ . In the simplest case of two lines this

amounts to an independent sample  $t$  test, while in the case of  $k > 2$  lines, the usual (Type III)  $F$  test (in the presence of the covariate) is used (with possibly a number of *post-hoc* comparisons). Note that

this test is given by 
$$F = \frac{SS(X,Z) - SS(Z)}{MSE(X,Z)} \sim F_{a-1, a(n-1)-1}$$

Example: Age-systolic blood pressure data. The systolic blood pressure is compared among males and females (Table 11-1 in text). The expectation is that males have different blood pressure from females, but the effect of age on blood pressure is also an important factor. The data set follows:

```

. by gender: list SBP age
-> gender=      Male
      SBP  age      SBP  age
1.   158  41  21.   150  38
2.   185  60  22.   156  52
3.   152  41  23.   134  41
4.   159  47  24.   134  18
5.   176  66  25.   174  51
6.   156  47  26.   174  55
7.   184  68  27.   158  65
8.   138  43  28.   144  33
9.   172  68  29.   139  23
10.  168  57  30.   180  70
11.  176  65  31.   165  56
12.  164  57  32.   172  62
13.  154  61  33.   160  51
14.  124  36  34.   157  48
15.  142  44  35.   170  59
16.  144  50  36.   153  40
17.  149  47  37.   148  35
18.  128  19  38.   140  33
19.  130  22  39.   132  26
20.  138  21  40.   169  61
-> gender=      Female
      SBP  age      SBP  age
1.   175  69  21.   120  39
2.   158  67  22.   136  36
3.   170  67  23.   110  34
4.   162  65  24.   130  29
5.   162  64  25.   125  25
6.   144  63  26.   120  21
7.   140  59  27.   116  20
8.   150  56  28.   124  19
9.   154  56  29.   114  17
10.  158  53
11.  142  50
12.  130  48
13.  145  47
14.  142  46
15.  135  45
16.  138  45
17.  160  44
18.  124  42
19.  128  42
20.  144  39

```

The comparison between males and females is conducted as follows:

```
. by gender: sum SBP age
```

-> gender= Male					
Variable	Obs	Mean	Std. Dev.	Min	Max
SBP	40	155.15	16.56618	124	185
age	40	46.925	14.87105	18	70

```
. by gender: sum SBP age
```

-> gender= Female					
Variable	Obs	Mean	Std. Dev.	Min	Max
SBP	29	139.8621	17.50454	110	175
age	29	45.06897	15.56078	17	69

```
. sum SBP age
```

Variable	Obs	Mean	Std. Dev.	Min	Max
SBP	69	148.7246	18.47565	110	185
age	69	46.14493	15.07947	17	70

The analysis points out a significant difference in mean systolic blood pressure between males and females. However, we must adjust for the age effect in both groups. The mean in the two groups is:

$\bar{Y}_M = 155.15$  for the males, and  $\bar{Y}_F = 139.86$  for the females.



The regression of systolic blood pressure (SBP) on age is conducted as follows:

```
. reg SBP age
```

Source	SS	df	MS	Number of obs = 69		
Model	14951.2546	1	14951.2546	F( 1, 67)	=	121.27
Residual	8260.51351	67	123.291246	Prob > F	=	0.0000
Total	23211.7681	68	341.349531	R-squared	=	0.6441
				Adj R-squared	=	0.6388
				Root MSE	=	11.104

SBP	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
age	.9833276	.0892947	11.012	0.000	.8050947	1.161561
_cons	103.3491	4.331896	23.858	0.000	94.70256	111.9956

Analysis of variance adjusted for the effect of age:

```
. anova SBP age gender, continuous(age) seq
```

```

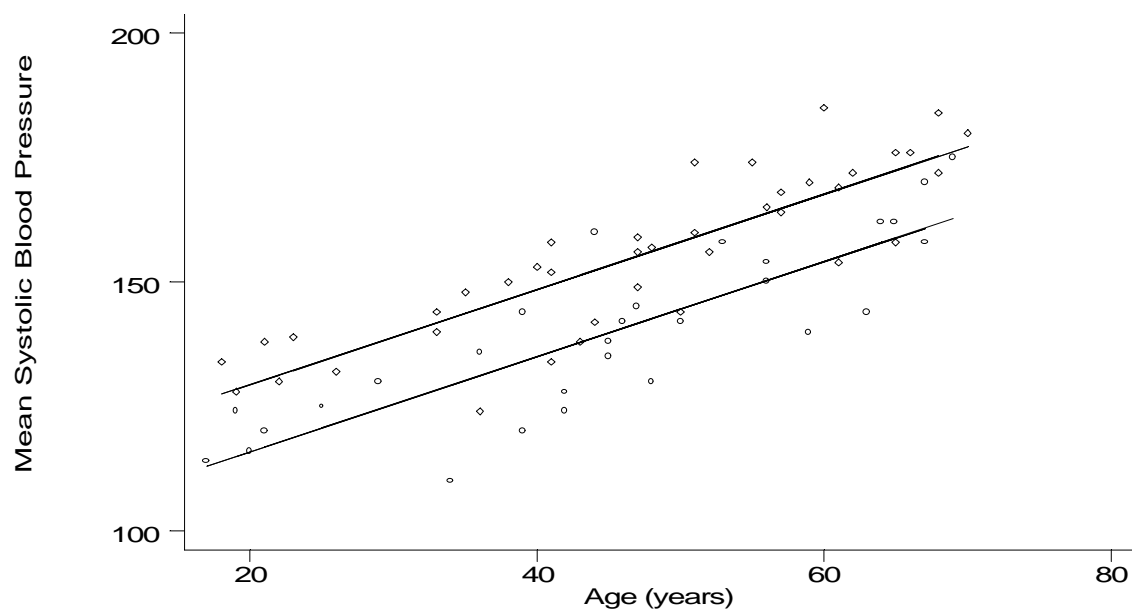
                Number of obs =      69      R-squared      =  0.7759
                Root MSE      = 8.87795     Adj R-squared =  0.7691

```

Source	Seq. SS	df	MS	F	Prob > F
Model	18009.7794	2	9004.88968	114.25	0.0000
age	14951.2546	1	14951.2546	189.69	0.0000
gender	3058.52475	1	3058.52475	38.80	0.0000
Residual	5201.98876	66	78.8180115		
Total	23211.7681	68	341.349531		

The plot of the data and the necessary STATA commands are as follows:

```
. predict sbphat
. gen shat0=sbphat if gender==0
. gen shat1=sbphat if gender==1
. gen sbp0=SBP if gender==0
. gen sbp1=SBP if gender==1
. label var sbp0 "Systolic Blood Pressure (females)"
. label var sbp1 "Systolic Blood Pressure (males)"
. graph shat0 shat1 sbp0 sbp1, c(ll..) s(iido) xlab ylab
    ll(Mean Systolic Blood Pressure)
    ◊ Systolic Blood Pressure (males) ◊ Systolic Blood Pressure (female)
```



**Comments:**

1. From the simple linear regression we have  $SS(\hat{\beta}_1) = S_{xy}^2 / S_{xx} = 14951.25$ , and the sums squares for the residual are  $SSE' = S_{yy} - S_{xy}^2 / S_{xx} = 3058.52$ .
2. The overall (from the whole data) estimate of the slope of systolic blood pressure with age is  $\hat{\beta}_1 = 0.9833$ , meaning that for every year of life, blood pressure increases 0.98 units on average.
3. From the ANOVA table, we see that the  $SS(\hat{\beta}_1) = S_{xy}^2 / S_{xx} = 14951.25$ . This is the same as the sum squares from a simple linear regression. The Type I sum of squares for the gender comparison is  $SS(\text{GENDER} | \hat{\beta}_1) = 3058.52$  leading to a statistically significant partial  $F = 38.80$ .
4. The  $S_y = \sqrt{MSE} = \sqrt{78.8180} = 8.878$ . This is smaller than the variance estimate that was produced by the ANOVA model without the age effect that was  $S'_y = \sqrt{123.2912} = 11.104$ , indicating that the adjustment of the analysis by the age effect was warranted.

Analysis of covariance with one effect and a single covariate

The analysis of covariance where both the gender and age effect are considered as adjustments is as follows:

```
. anova SBP age gender, continuous(age)
```

```

                Number of obs =      69      R-squared      =  0.7759
                Root MSE      = 8.87795      Adj R-squared =  0.7691

```

Source	Partial SS	df	MS	F	Prob > F
Model	18009.7794	2	9004.88968	114.25	0.0000
age	14080.5595	1	14080.5595	178.65	0.0000
gender	3058.52475	1	3058.52475	38.80	0.0000
Residual	5201.98876	66	78.8180115		
Total	23211.7681	68	341.349531		

In order to obtain the regression estimates for age we add the option `regress` in the previous `anova` command as follows:

```
. reg
```

Source	SS	df	MS			
Model	18009.7794	2	9004.88968	Number of obs =	69	
Residual	5201.98876	66	78.8180115	F( 2, 66) =	114.25	
Total	23211.7681	68	341.349531	Prob > F =	0.0000	
				R-squared =	0.7759	
				Adj R-squared =	0.7691	
				Root MSE =	8.878	

SBP	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
_cons	96.77353	3.620854	26.727	0.000	89.54426	104.0028
age	.956058	.0715298	13.366	0.000	.8132441	1.098872
gender						
1	13.51345	2.169318	6.229	0.000	9.182273	17.84464
2	(dropped)					

**Comments:**

1. The partial sums of squares  $SS(\text{AGE}|\text{GENDER})=14080.56$ ,  $SS(\text{GENDER}|\text{AGE})=3058.52$ . These lead to Type III  $F$  statistics  $F(\text{AGE}|\text{GENDER})=178.65$  and  $F(\text{GENDER}|\text{AGE})=38.80$ , both of which are statistically significant.
2. The estimate of the common slope between males and females is given in the output of the regression model as  $\hat{\beta}_1=0.9561$  which is slightly less than 0.9833, the unadjusted estimate of the slope from the simple linear regression of SBP on age.
3. We saw previously that the raw (unadjusted) mean SBP for females and males were  $\bar{Y}_F=139.86$  and  $\bar{Y}_M=155.15$  respectively. The *adjusted* (for the effect of age) mean SBP for females and males are respectively  $\bar{Y}_{F\text{adj.}}=\bar{Y}_F-\hat{\beta}_1(\bar{X}_F.-\bar{X}_{..})=139.86-0.9561(45.069-46.144)=140.89$  and  $\bar{Y}_{M\text{adj.}}=\bar{Y}_M-\hat{\beta}_1(\bar{X}_M.-\bar{X}_{..})=155.15-0.9561(46.925-46.144)=154.40$ . Thus, adjustment for the age of the two groups produced a slight adjustment in the mean SBP in each group.

If we want to investigate the presence of interaction between age and gender we use the following model:

```
. anova SBP age gender age*gender, continuous(age)
```

	Number of obs =	69	R-squared =	0.7759
	Root MSE =	8.94551	Adj R-squared =	0.7656

Source	Partial SS	df	MS	F	Prob > F
Model	18010.3287	3	6003.4429	75.02	0.0000
age	13857.691	1	13857.691	173.17	0.0000
gender	273.443297	1	273.443297	3.42	0.0691
age*gender	.549356192	1	.549356192	0.01	0.9342
Residual	5201.4394	65	80.0221447		
Total	23211.7681	68	341.349531		



To obtain the regression estimates for age we add the option `regress` in the previous `anova` command as follows:

```
. reg
```

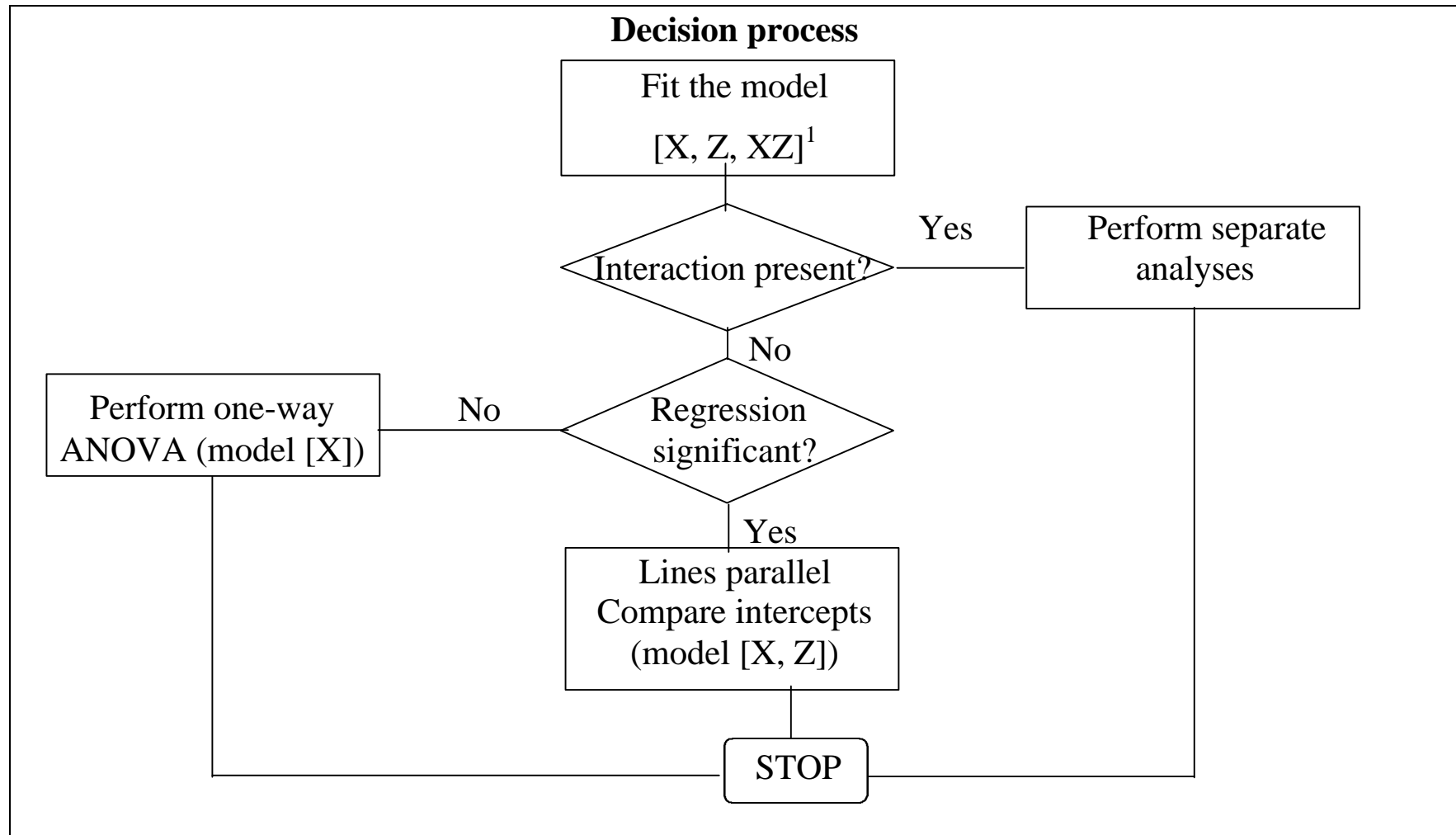
Source	SS	df	MS	Number of obs = 69		
Model	18010.3287	3	6003.4429	F( 3, 65)	=	75.02
Residual	5201.4394	65	80.0221447	Prob > F	=	0.0000
Total	23211.7681	68	341.349531	R-squared	=	0.7759
				Adj R-squared	=	0.7656
				Root MSE	=	8.9455

SBP	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
_cons	97.07708	5.170455	18.775	0.000	86.75097	107.4032
age	.9493225	.1086412	8.738	0.000	.732351	1.166294
gender						
1	12.96144	7.011725	1.849	0.069	-1.041936	26.96482
2	(dropped)					
age*gender						
1	.0120301	.1451933	0.083	0.934	-.2779409	.3020011
2	(dropped)					

**Comments:**

1. By our assumptions ( $\sum_{i=1}^a \tau_i = 0$  and  $\sum_{i=1}^a \gamma_i = 0$ ), only one degree of freedom is associated with the effect  $\tau$  (gender) and interaction  $\gamma_i$  age\*gender. Their levels are *deviations* from overall quantities  $\mu$  and  $\beta$  respectively. STATA defines the level with the largest coded value defines as the reference level, (female -- gender=1) so,  $\hat{\beta}_F = 0.9493 = \hat{\beta}$  (i.e.,  $\hat{\gamma}_F = 0$ ),  $\hat{\beta}_{oF} = 97.007 = \hat{\mu}$ , (i.e.,  $\hat{\tau}_F = 0$ ),  $\hat{\beta}_M = 0.9613 = 0.9493 + 0.0120 = \hat{\beta} + \hat{\gamma}_M$   $\hat{\beta}_{oM} = 109.968 = 97.007 + (12.961) = \hat{\mu} + \hat{\tau}_{AM}$
2. A crucial point is that in this statistical model the  $t$  test is not equivalent to the Type III  $F$  test and the estimates are dependent on the coding of the variable gender. Here male=0 and female=1. However, had we coded male=1 and female=0, then  $\hat{\beta} = 0.9613 = \hat{\beta}_M$ , while  $\hat{\beta}_F = 0.9613 - 0.0120 = 0.9493$ . A variation of this model that produces  $t$  tests exactly equivalent to the partial  $F$  tests will be considered during the next lecture.
3. Since interaction is not significant, the assumption of parallelism holds. We must return to the previous analysis without interaction (presented in the regression output and the figure above).



<sup>1</sup> This is the full model containing the interaction term  $XZ$ , the main effect  $X$  and the covariate  $Z$