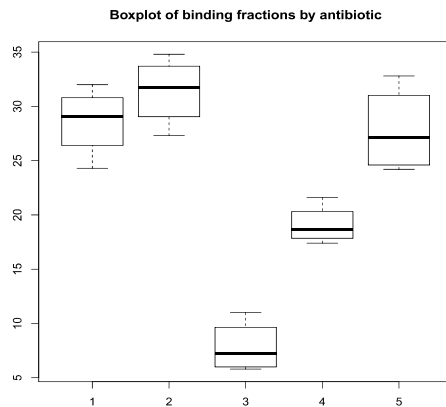


Single factor experiments

Following data come from study investigating binding fraction for several antibiotics using $n = 20$ bovine serum samples:



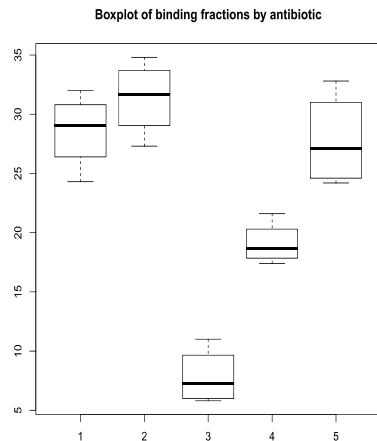
Antibiotic	Binding Percentage				Sample mean	Sample s.d.
Penicillin G	29.6	24.3	28.5	32	28.6	3.2
Tetracyclin	27.3	32.6	30.8	34.8	31.4	3.2
Streptomycin	5.8	6.2	11	8.3	7.8	2.4
Erythromycin	21.6	17.4	18.3	19	19.1	1.8
Chloramphenicol	29.2	32.8	25	24.2	27.8	4.0

A _____ (CRD) was used.

(All assignment of antibiotics to serum samples equally likely.)

Q: Are the population means for these 5 treatments plausibly equal?

Q: Do these (sample) treatment means differ significantly?



```
> bf.dat <- read.table("bindingfractions.txt",header=T)
> with(bf.dat,
+ boxplot(y~drug,main="Boxplot of binding fractions by
+ antibiotic"))
> dev.copy2pdf(file="bindingfractions.pdf")
X11cairo
      2
```

```
> bf.dat$drug <- as.factor(bf.dat$drug)
> bf.out <- lm(bf.dat$y ~ bf.dat$drug)
> anova(bf.out)
Analysis of Variance Table

Response: bf.dat$y
          Df  Sum Sq Mean Sq F value    Pr(>F)
bf.dat$drug  4 1480.82   370.21  40.885 6.74e-08 ***
Residuals   15   135.82     9.05
---
Signif. codes:  0   ***    0.001   **    0.01   *    0.05   .    0.1
```

An ANOVA table. Note that $df = 4$.

Modelling the binding fraction expt

“Effects” model parameterizes antibiotic effects as differences from mean:

$$Y_{ij} = \mu + \tau_i + E_{ij}$$

for $i = 1, \dots, 5$ and $j = 1, \dots, 4$, where E_{ij} are i.i.d. $N(0, \sigma^2)$ errors.

- μ - overall population mean (avg of 5 treatment population means)
- τ_i - difference between (population) mean for treatment i and μ
- σ^2 - (population) variance of bf for a given antibiotic

To test H_0 : _____ = 0, we just carry out one-way ANOVA:

Source	d.f.	Sum of squares	Mean Square	F	p-value
Treatments	4	1481	370	41	
Error	15	136	9		
Total	19	1617			

Conclusion? (Use $F(0.05, 4, 15) = 3.06$)

Parameter estimates $\hat{\mu}, \hat{\tau}_1, \hat{\tau}_2, \hat{\tau}_3, \hat{\tau}_4, \hat{\tau}_5$? *Six parameters. Not uniquely estimable*

$$\widehat{\mu + \tau_1} = \bar{y}_{1.} = 28.6, \dots, \widehat{\mu + \tau_5} = \bar{y}_{5.} = 27.8$$

Standard errors of parameter estimates?

$$\text{StdErr}(\widehat{\mu + \tau_i}) = \text{StdErr}(\bar{y}_{i.}) = \underline{\hspace{2cm}}$$

Table for balanced one-way ANOVA

Y_{ij} denotes j^{th} observation receiving level i of treatment factor with t levels, for a total of N observations.

Source	d.f.	Sum of squares	Mean Square	F
Treatments	$t - 1$	$SS[T]$	$MS[T] = \frac{SS[T]}{(t-1)}$	$F = \frac{MS[T]}{MS[E]}$
Error	$N - t$	$SS[E]$	$MS[E] = \frac{SS[E]}{(N-t)}$	
Total	$N - 1$	$SS[TOT]$		

where

$$SS[T] = \sum \sum (\bar{y}_{i+} - \bar{y}_{..})^2$$

$$SS[E] = \sum \sum (y_{ij} - \bar{y}_{i+})^2$$

$$SS[TOT] = \sum \sum (y_{ij} - \bar{y}_{..})^2$$

The linear model $\mu_{ij} = E(Y_{ij}) = \mu + \tau_i$ could be fit using MLR with 5 **indicator variables** x_1, \dots, x_5 for the 5 antibiotics. Let

$$x_{ij} = \begin{cases} 1 & \text{if treatment } j \\ 0 & \text{else} \end{cases}$$

A general linear model

Models which parameterize the effects of classification factors this way are general linear models. One-way ANOVA and linear regression models are general linear models. The linearity pertains to the parameters, not the explanatory variables.

Here, reparameterizing using 5 – 1 indicator variables leads to a general linear model. Define x_1, x_2, x_3, x_4 as before. Then the MLR model is

$$Y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3} + \beta_4 x_{i4} + E_i \quad i = 1, \dots, 20$$

where $E_i \stackrel{iid}{\sim} N(0, \sigma^2)$.

The X matrix looks like

$$X = \begin{pmatrix} 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \end{pmatrix}$$

Remarks:

- $(X'X)^{-1}$ exists
- continuously valued covariates (as opposed to indicators) can be added and it is still a general linear model

For the one-way ANOVA,

$$\hat{\beta} = (X'X)^{-1}X'Y = \begin{pmatrix} 27.8 \\ 0.8 \\ 3.6 \\ -20.0 \\ -8.7 \end{pmatrix}$$

Estimates for the five treatment means obtained by substitution of $\hat{\beta}$ into $\mu(x_1, x_2, x_3, x_4) = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3 + \beta_4x_4$

$\hat{\mu}(1, 0, 0, 0)$	$=$	$(1, 1, 0, 0, 0)\hat{\beta}$	$=$	$\hat{\beta}_0 + \hat{\beta}_1$	$=$	28.6
$\hat{\mu}(0, 1, 0, 0)$	$=$	$(1, 0, 1, 0, 0)\hat{\beta}$	$=$	$\hat{\beta}_0 + \hat{\beta}_2$	$=$	31.4
$\hat{\mu}(0, 0, 1, 0)$	$=$	$(1, 0, 0, 1, 0)\hat{\beta}$	$=$	$\hat{\beta}_0 + \hat{\beta}_3$	$=$	7.8
$\hat{\mu}(0, 0, 0, 1)$	$=$	$(1, 0, 0, 0, 1)\hat{\beta}$	$=$	_____	$=$	_____
$\hat{\mu}(0, 0, 0, 0)$	$=$	$(1, 0, 0, 0, 0)\hat{\beta}$	$=$	_____	$=$	27.8

(Compare with slide 1.)

For standard errors, use $\hat{\Sigma}$:

$$\hat{\Sigma} = MS[E](X'X)^{-1} = \begin{pmatrix} 2.26 & -2.26 & -2.26 & -2.26 & -2.26 \\ & 4.53 & 2.26 & 2.26 & 2.26 \\ & & 4.53 & 2.26 & 2.26 \\ & & & 4.53 & 2.26 \\ & & & & 4.53 \end{pmatrix}$$

Let a, b, c, d be defined by

$$a' = (1, 1, 0, 0, 0), b' = (1, 0, 1, 0, 0), c' = (1, 0, 0, 1, 0), d' = (1, 0, 0, 0, 1).$$

Then

$$\begin{aligned} \hat{\mu}(1, 0, 0, 0) &= \hat{\beta}_0 + \hat{\beta}_1 = a' \hat{\beta} \\ \hat{\mu}(0, 1, 0, 0) &= \hat{\beta}_0 + \hat{\beta}_2 = b' \hat{\beta} \\ \hat{\mu}(0, 0, 1, 0) &= \hat{\beta}_0 + \hat{\beta}_3 = c' \hat{\beta} \\ \hat{\mu}(0, 0, 0, 1) &= \hat{\beta}_0 + \hat{\beta}_4 = d' \hat{\beta} \\ \hat{\mu}(0, 0, 0, 0) &= \hat{\beta}_0 = \hat{\beta}_0 \end{aligned}$$

and

$$a' \hat{\Sigma} a = b' \hat{\Sigma} b = c' \hat{\Sigma} c = d' \hat{\Sigma} d = \hat{\Sigma}_{11} = 2.3 = \widehat{\text{Var}}(\hat{\beta}_0) = \widehat{\text{Var}}(\hat{\beta}_0 + \hat{\beta}_j)$$

so the estimated SE for any sample treatment mean is $\sqrt{2.3} = 1.5$.

Checking matrix arithmetic:

$$\begin{aligned}
 (1, 1, 0, 0, 0) \widehat{\Sigma} \begin{pmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{pmatrix} &= \\
 &= (1, 1, 0, 0, 0) \begin{pmatrix} 2.26 & -2.26 & -2.26 & -2.26 & -2.26 \\ & 4.53 & 2.26 & 2.26 & 2.26 \\ & & 4.53 & 2.26 & 2.26 \\ & & & 4.53 & 2.26 \\ & & & & 4.53 \end{pmatrix} \begin{pmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{pmatrix} \\
 &= (0, 2.26, 0, 0, 0) \begin{pmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \\
 &= 2.26
 \end{aligned}$$

$$\widehat{SE}(\widehat{\beta}_0 + \widehat{\beta}_1) = \sqrt{2.26} = 1.5 = \sqrt{MS(E)/4}$$

(Same for all sample treatment means in balanced experiment.)


```

proc glm data=one;
  class drug;
  model y=drug/solution inv;
run;

```

The SAS System
The GLM Procedure

Class Level Information

Class	Levels	Values
drug	5	1 2 3 4 5

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	1480.823000	370.205750	40.88	<.0001
Error	15	135.822500	9.054833		
Corrected Total	19	1616.645500			

R-Square	Coeff Var	Root MSE	y Mean
0.915985	13.12023	3.009125	22.93500

Source	DF	Type I SS	Mean Square	F Value	Pr > F
drug	4	1480.823000	370.205750	40.88	<.0001

Parameter	Estimate	Standard Error	t Value	Pr > t
Intercept	27.80000000 B	1.50456251	18.48	<.0001
drug 1	0.80000000 B	2.12777270	0.38	0.7122
drug 2	3.57500000 B	2.12777270	1.68	0.1136
drug 3	-19.97500000 B	2.12777270	-9.39	<.0001
drug 4	-8.72500000 B	2.12777270	-4.10	0.0009
drug 5	0.00000000 B	.	.	.

NOTE: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter 'B' are not uniquely estimable.

$$y = \begin{pmatrix} 29.6 \\ 24.3 \\ 28.5 \\ 32.0 \\ 27.3 \\ 32.6 \\ 30.8 \\ 34.8 \\ 5.8 \\ 6.2 \\ 11.0 \\ 8.3 \\ 21.6 \\ 17.4 \\ 18.3 \\ 19.0 \\ 29.2 \\ 32.8 \\ 25.0 \\ 24.2 \end{pmatrix}, X = \begin{pmatrix} 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \beta = \begin{pmatrix} \mu \\ \tau_1 \\ \tau_2 \\ \tau_3 \\ \tau_4 \\ \tau_5 \end{pmatrix},$$

$$X'X = \begin{pmatrix} 20 & 4 & 4 & 4 & 4 & 4 \\ 4 & 4 & 0 & 0 & 0 & 0 \\ 4 & 0 & 4 & 0 & 0 & 0 \\ 4 & 0 & 0 & 4 & 0 & 0 \\ 4 & 0 & 0 & 0 & 4 & 0 \\ 4 & 0 & 0 & 0 & 0 & 4 \end{pmatrix}$$

Add rows 2-6 of $X'X$. $(X'X)^{-1}$?

NOTE: The $X'X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter 'B' are not uniquely estimable.

Class Level Information							
Class	Levels	Values					
drug	5	1	2	3	4	5	
X'X Generalized Inverse (g2)							
	Intercept	drug 1	drug 2	drug 3	drug 4	drug 5	y
Intercept	0.25	-0.25	-0.25	-0.25	-0.25	0	27.8
drug 1	-0.25	0.5	0.25	0.25	0.25	0	0.8
drug 2	-0.25	0.25	0.5	0.25	0.25	0	3.575
drug 3	-0.25	0.25	0.25	0.5	0.25	0	-19.975
drug 4	-0.25	0.25	0.25	0.25	0.5	0	-8.725
drug 5	0	0	0	0	0	0	0

A generalized inverse, of a matrix A , A^- has this property: $AA^-A = A$.

$$(X'X)^- X'Y = \begin{pmatrix} 0.25 & -0.25 & -0.25 & -0.25 & -0.25 & 0 \\ -0.25 & 0.5 & 0.25 & 0.25 & 0.25 & 0 \\ -0.25 & 0.25 & 0.5 & 0.25 & 0.25 & 0 \\ -0.25 & 0.25 & 0.25 & 0.5 & 0.25 & 0 \\ -0.25 & 0.25 & 0.25 & 0.25 & 0.5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} 458.7 \\ 114.4 \\ 125.5 \\ 31.3 \\ 76.3 \\ 111.2 \end{pmatrix} = \begin{pmatrix} 27.800 \\ 0.800 \\ 3.575 \\ -19.975 \\ -8.725 \\ 0 \end{pmatrix}$$

$$= \begin{pmatrix} \widehat{\mu + \tau_5} \\ \widehat{\tau_1 - \tau_5} \\ \widehat{\tau_2 - \tau_5} \\ \widehat{\tau_3 - \tau_5} \\ \widehat{\tau_4 - \tau_5} \end{pmatrix}$$

The $\widehat{\tau}_i$ are not uniquely estimable, and will change with different choices for the generalized inverse, $(X'X)^-$, but $\widehat{\mu + \tau_i}$ (and many other functions of interest), are uniquely estimable, and will not change with different generalized inverses.

Generalized inverse corresponding to dropped 5th row:

The REG Procedure

Model: MODEL1

Model Crossproducts X'X X'Y Y'Y

Variable	Intercept	x1	x2	x3	x4	y
Intercept	20	4	4	4	4	458.7
x1	4	4	0	0	0	114.4
x2	4	0	4	0	0	125.5
x3	4	0	0	4	0	31.3
x4	4	0	0	0	4	76.3
y	458.7	114.4	125.5	31.3	76.3	12136.93

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	27.80000	1.50456	18.48	<.0001
x1	1	0.80000	2.12777	0.38	0.7122
x2	1	3.57500	2.12777	1.68	0.1136
x3	1	-19.97500	2.12777	-9.39	<.0001
x4	1	-8.72500	2.12777	-4.10	0.0009

Generalized inverse corresponding to dropped 1st row:

The REG Procedure
Model: MODEL2

Model Crossproducts X'X X'Y Y'Y						
Variable	Intercept	x2	x3	x4	x5	y
Intercept	20	4	4	4	4	458.7
x2	4	4	0	0	0	125.5
x3	4	0	4	0	0	31.3
x4	4	0	0	4	0	76.3
x5	4	0	0	0	4	111.2
y	458.7	125.5	31.3	76.3	111.2	12136.93

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	28.60000	1.50456	19.01	<.0001
x2	1	2.77500	2.12777	1.30	0.2118
x3	1	-20.77500	2.12777	-9.76	<.0001
x4	1	-9.52500	2.12777	-4.48	0.0004
x5	1	-0.80000	2.12777	-0.38	0.7122

Generalized inverse corresponding to dropped 2nd row:

The REG Procedure

Model: MODEL3

Model Crossproducts X'X X'Y Y'Y

Variable	Intercept	x1	x3	x4	x5	y
Intercept	20	4	4	4	4	458.7
x1	4	4	0	0	0	114.4
x3	4	0	4	0	0	31.3
x4	4	0	0	4	0	76.3
x5	4	0	0	0	4	111.2
y	458.7	114.4	31.3	76.3	111.2	12136.93

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	31.37500	1.50456	20.85	<.0001
x1	1	-2.77500	2.12777	-1.30	0.2118
x3	1	-23.55000	2.12777	-11.07	<.0001
x4	1	-12.30000	2.12777	-5.78	<.0001
x5	1	-3.57500	2.12777	-1.68	0.1136

Generalized inverse corresponding to dropped 3rd row:

The REG Procedure

Model: MODEL4

Model Crossproducts X'X X'Y Y'Y

Variable	Intercept	x1	x2	x4	x5	y
Intercept	20	4	4	4	4	458.7
x1	4	4	0	0	0	114.4
x2	4	0	4	0	0	125.5
x4	4	0	0	4	0	76.3
x5	4	0	0	0	4	111.2
y	458.7	114.4	125.5	76.3	111.2	12136.93

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	7.82500	1.50456	5.20	0.0001
x1	1	20.77500	2.12777	9.76	<.0001
x2	1	23.55000	2.12777	11.07	<.0001
x4	1	11.25000	2.12777	5.29	<.0001
x5	1	19.97500	2.12777	9.39	<.0001

Generalized inverse corresponding to dropped 4th row:

The REG Procedure

Model: MODEL5

Model Crossproducts X'X X'Y Y'Y

Variable	Intercept	x1	x2	x3	x5	y
Intercept	20	4	4	4	4	458.7
x1	4	4	0	0	0	114.4
x2	4	0	4	0	0	125.5
x3	4	0	0	4	0	31.3
x5	4	0	0	0	4	111.2
y	458.7	114.4	125.5	31.3	111.2	12136.93

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	19.07500	1.50456	12.68	<.0001
x1	1	9.52500	2.12777	4.48	0.0004
x2	1	12.30000	2.12777	5.78	<.0001
x3	1	-11.25000	2.12777	-5.29	<.0001
x5	1	8.72500	2.12777	4.10	0.0009

Generalized inverse corresponding to dropped intercept

The REG Procedure
Model: MODEL6

Model Crossproducts X'X X'Y Y'Y

Variable	x1	x2	x3	x4	x5	y
x1	4	0	0	0	0	114.4
x2	0	4	0	0	0	125.5
x3	0	0	4	0	0	31.3
x4	0	0	0	4	0	76.3
x5	0	0	0	0	4	111.2
y	114.4	125.5	31.3	76.3	111.2	12136.93

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
x1	1	28.60000	1.50456	19.01	<.0001
x2	1	31.37500	1.50456	20.85	<.0001
x3	1	7.82500	1.50456	5.20	0.0001
x4	1	19.07500	1.50456	12.68	<.0001
x5	1	27.80000	1.50456	18.48	<.0001

As an exercise, obtain the least squares estimate of $\mu + \tau_1$ and $\theta_2 = \tau_2 - \tau_1$ using each generalized inverse:

Gen'd Inverse	$\widehat{\mu + \tau_1}$	$\widehat{\tau_2 - \tau_1}$
1	$27.8 + 0.8 = 28.6$	$3.575 - 0.8 = 2.775$
2	$28.6 + 0 = 28.6$	$2.775 - 0.0 = 2.775$
3	$31.375 - 2.775 = 28.6$	$0 - (-2.775) = 2.775$
4		
5		
6		

Apparently, μ, τ_1, \dots are not uniquely estimable, but $\mu + \tau_1$ and $\tau_2 - \tau_1$ are.

Complete this table as an exercise.

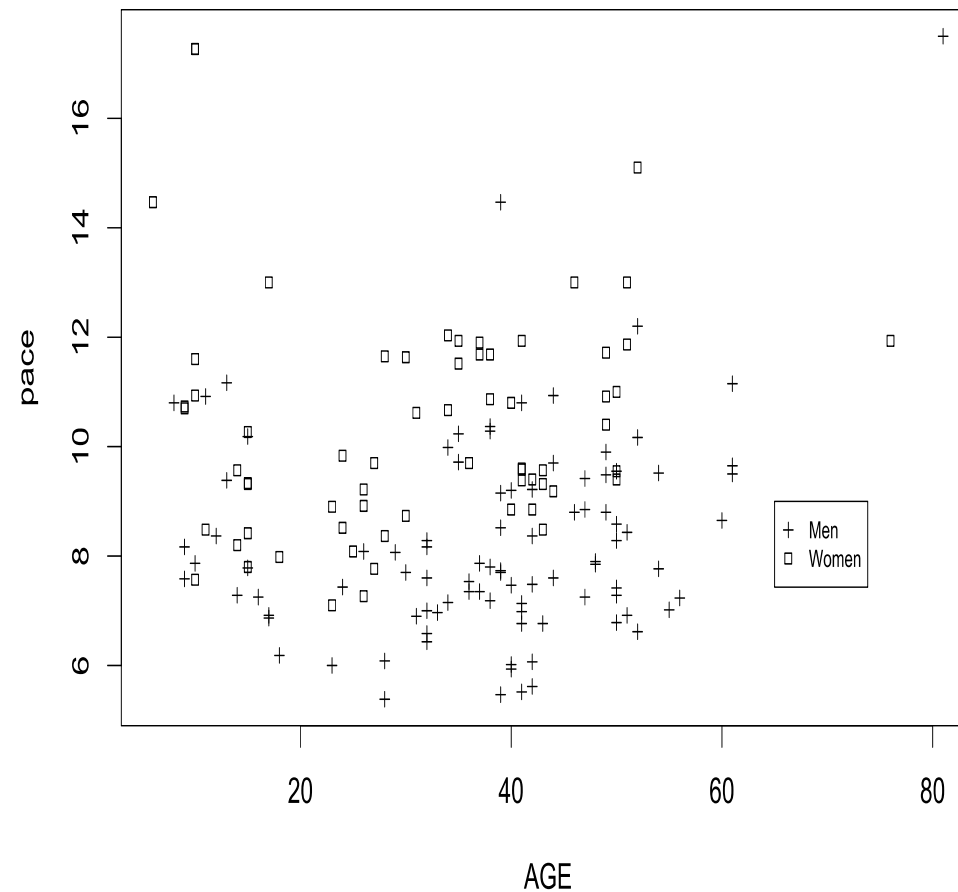
Estimable functions of regression coefficients

- Definition: In the general linear model, $Y = X\beta + E$, a linear combination of parameters, $\lambda'\beta$ is said to be _____ if there exists a linear combination of the data, $a'Y$ with that as its expectation, so that $E(a'Y) = \lambda'\beta$. If no such linear combination exists, $\lambda'\beta$ is nonestimable.
 - If $\lambda \in \text{rowsp}(X)$ then $\lambda'\beta$ is estimable. (λ can be obtained as a linear combination of the rows of X .)
- 1 Is $\lambda'\beta$ estimable where $\lambda' = (1, 1, 0, 0, 0, 0)$ _____ Which rows of X ?
 - 2 Is $\lambda'\beta$ estimable where $\lambda' = (0, -1, 1, 0, 0, 0)$ _____ Which rows of X ?
 - 3 Is $\lambda'\beta$ estimable where $\lambda' = (0, 1, 0, 0, 0, 0)$ _____ Which rows of X ?

A general linear model

Both indicator variables for factorial effects (sex) as well as continuously valued variables (age, age squared).

Resolution Run (5k), 1/1/2004



Quadratic model $\mu(x) = \beta_0 + \beta_1x + \beta_1x^2$ used for association between mean pace and age. How could the model be extended to incorporate sex differences? Let $x_2 = x^2$ and let an indicator variable x_3 be defined by

$$x_3 = \begin{cases} 1 & \text{female} \\ 0 & \text{male} \end{cases}$$

Some candidate models:

$$\mu(x_1, x_2, x_3) = \beta_0$$

$$\mu(x_1, x_2, x_3) = \beta_0 + \beta_3x_3$$

$$\mu(x_1, x_2, x_3) = \beta_0 + \beta_1x_1$$

$$\mu(x_1, x_2, x_3) = \beta_0 + \beta_1x_1 + \beta_2x_2$$

$$\mu(x_1, x_2, x_3) = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3$$

$$\mu(x_1, x_2, x_3) = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3 + \beta_4 \underbrace{x_1x_3}_{x_4} + \beta_5 \underbrace{x_2x_3}_{x_5}$$

```

data race5k; set race5k;
    sexf=(sex="F"); age2=age*age;  agef=age*sexf;  age2f=age2*sexf;
proc reg data=one ;
    model pace=;
    model pace=sexf; /* equivalent to two-sample t-test */
    model pace=age age2;
    model pace=sexf age age2;
    model pace=sexf age age2 agef age2f;
    test agef=0, age2f=0;
run;

```

The REG Procedure
Model: MODEL1

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	0	0	.	.	.
Error	159	788.09472	4.95657		
Corrected Total	159	788.09472			

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	9.12063	0.17601	51.82	<.0001

Model: MODEL2

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	170.74137	170.74137	43.70	<.0001
Error	158	617.35335	3.90730		
Corrected Total	159	788.09472			

Root MSE 1.97669 R-Square 0.2167

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	8.26614	0.20280	40.76	<.0001
sexf	1	2.10335	0.31819	6.61	<.0001

Model: MODEL4

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	2	113.64500	56.82250	13.23	<.0001
Error	157	674.44972	4.29586		
Corrected Total	159	788.09472			

Root MSE 2.07265 R-Square 0.1442

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	11.78503	0.70216	16.78	<.0001
age	1	-0.19699	0.04113	-4.79	<.0001
age2	1	0.00294	0.00057380	5.12	<.0001

Model: MODEL5

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	290.34851	96.78284	30.33	<.0001
Error	156	497.74621	3.19068		
Corrected Total	159	788.09472			

Root MSE 1.78625 R-Square 0.3684

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	10.18317	0.64228	15.85	<.0001
sexf	1	2.19792	0.29535	7.44	<.0001
age	1	-0.17146	0.03562	-4.81	<.0001
age2	1	0.00281	0.00049481	5.67	<.0001

$$\mu(x) = \begin{cases} 10.18 - 0.17x + 0.0028x^2 & \text{for men} \\ \text{_____} & \text{for women} \end{cases}$$

Model: MODEL6

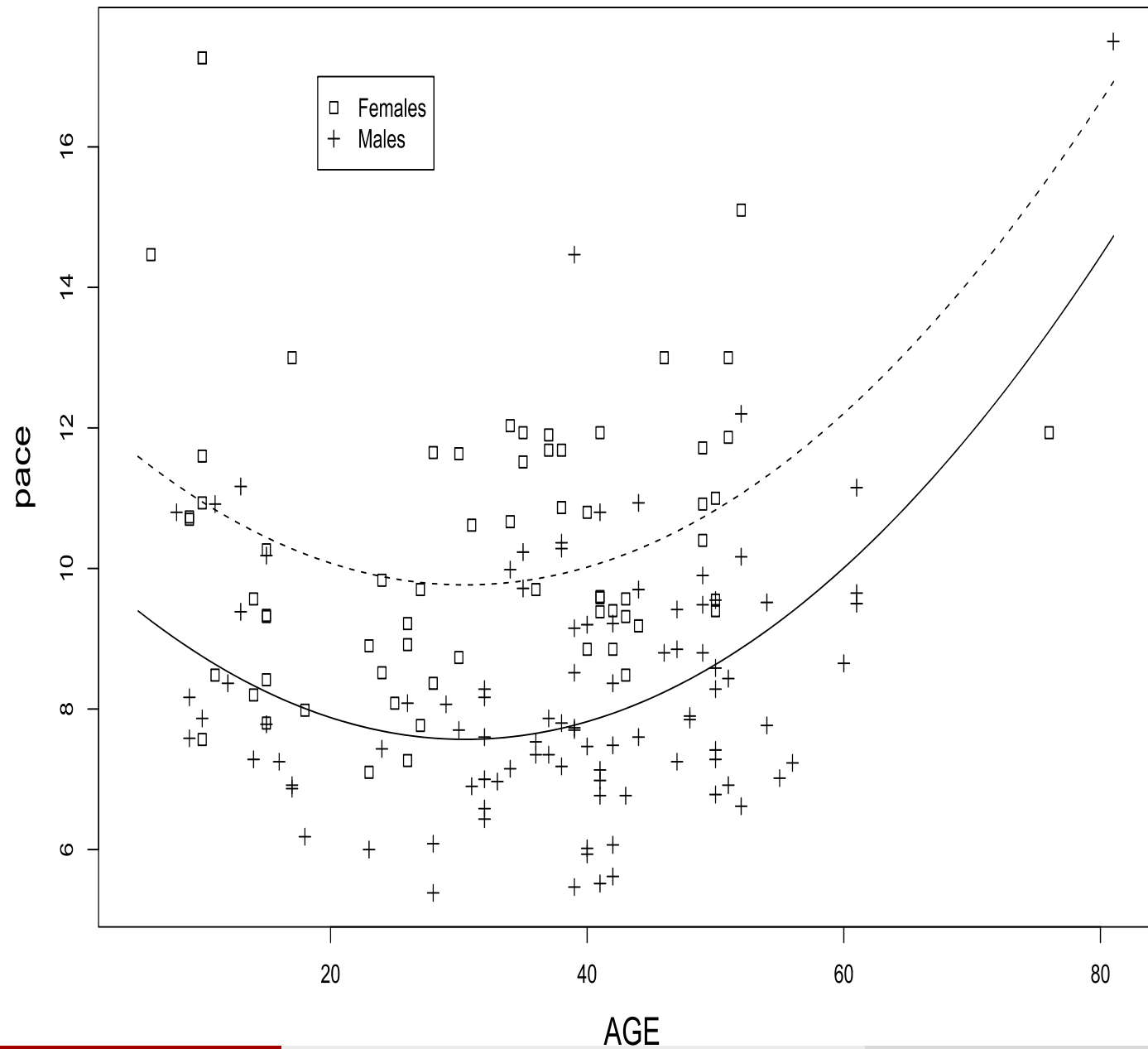
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	293.52828	58.70566	18.28	<.0001
Error	154	494.56644	3.21147		
Corrected Total	159	788.09472			

Root MSE 1.79206 R-Square 0.3725

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	1	10.60848	0.88641	11.97	<.0001
sexf	1	1.25728	1.23237	1.02	0.3092
age	1	-0.19986	0.04842	-4.13	<.0001
age2	1	0.00321	0.00064628	4.96	<.0001
agef	1	0.06882	0.07298	0.94	0.3471
age2f	1	-0.00103	0.00103	-0.99	0.3217

$$\mu(x) = \begin{cases} \beta_0 + \beta_1 x + \beta_2 x^2 + \beta_3(0) + \beta_4(0) + \beta_5(0) & \text{men} \\ \beta_0 + \beta_1 x + \beta_2 x^2 + \beta_3(1) + \beta_4(x) + \beta_5(x^2) & \text{women} \\ \beta_0 + \beta_3 + (\beta_1 + \beta_4)x + (\beta_2 + \beta_5)x^2 & \\ 10.61 + 1.25 + (-0.20 + 0.07)x + (0.0032 - 0.0010)x^2 & \\ 11.86 - 0.13x + 0.0022x^2 & \end{cases}$$

Model 5



Comparison of models 5 and 6

$$\text{reduced: } \mu(x_1, x_2, x_3) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3$$

$$\text{full: } \mu(x_1, x_2, x_3) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_1 x_3 + \beta_5 x_2 x_3$$

Extra sum of squares:

$$R(\beta_4, \beta_5 | \beta_0, \beta_1, \beta_2, \beta_3) = SS[R]_f - SS[R]_r = 293.5 - 290.3 = 3.0$$

The F -ratio

$$F = \frac{R(\beta_4, \beta_5 | \beta_0, \beta_1, \beta_2, \beta_3) / (5 - 3)}{MS[E]_f} = \frac{3.2/2}{3.21} = \frac{1.6}{3.21} = 0.5$$

The observed F -ratio is not significant on $df = 2, 154$.

In SAS, you could use

```
proc reg;  
  model pace=age age2 sexf agef age2f;  
  test agef=0, age2f=0;  
run;
```

to get the following model selection F -ratio in the output:

```
The REG Procedure  
Model: MODEL6
```

```
Test 1 Results for Dependent Variable pace
```

Nonlinear functions of parameters

Estimate “peak” running age for men/women. θ_M and θ_W denote peak running ages for men and women respectively. Using calculus on the model 6 regression,

$$\theta_M = \text{—————}, \quad \theta_W = \text{—————}$$

These are nonlinear functions of regression parameters. Note that acceptance of any model but 6 implies equality of these peak ages.

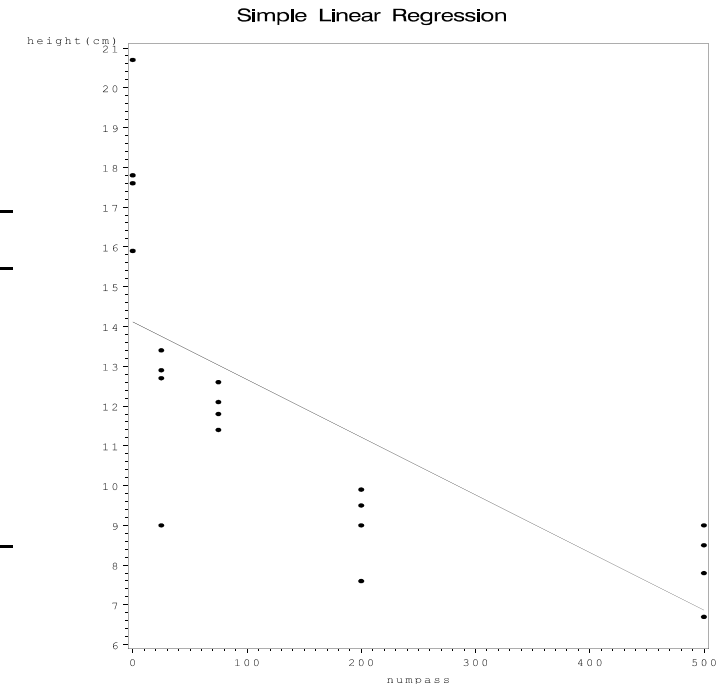
$$\hat{\theta}_W = \begin{cases} 30.5 & \text{different intercepts model (5)} \\ 30.1 & \text{full model (6)} \end{cases}$$

$$\hat{\theta}_M = \begin{cases} 30.5 & \text{different intercepts model (5)} \\ 31.1 & \text{full model (6)} \end{cases}$$

Lack-of-fit of a polynomial regression model

Completely randomized experiment in White Mountains of NH. $n = 20$ lanes of dimension $0.5m \times 1.5m$ randomized to 5 foot-traffic treatments:

i : trt grp	x : # of passes	y_{ij} : Height(cm)			
1	0	20.7	15.9	17.8	17.6
2	25	12.9	13.4	12.7	9.0
3	75	11.8	12.6	11.4	12.1
4	200	7.6	9.5	9.9	9.0
5	500	7.8	9.0	8.5	6.7



Two models for mean plant height:

$$\text{SLR model : } \mu(x) = \beta_0 + \beta_1 x_i$$

$$\text{one-factor ANOVA model : } \mu_{ij} = \mu + \tau_i$$

```

proc reg data=one;
    model y=numpass;

proc glm data=one;          *find the F-ratio that compares SLR with one-factor model;
    class cnumpass;        *find SS(Trt);
    model y=numpass cnumpass;      run;

```

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	141.29532	141.29532	19.15	0.0004
Error	18	132.79418	7.37745		
Corrected Total	19	274.08950			

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t
Intercept	Intercept	1	14.11334	0.80592	17.51	<.0001
numpass		1	-0.01449	0.00331	-4.38	0.0004

The GLM Procedure

Class		Levels	Values							
cnumpass		5	0	25	75	200	500			
		Sum of								
Source	DF	Squares	Mean Square		F	Value	Pr > F			
Model	4	243.1620000	60.7905000		29.48	<.0001				
Error	15	30.9275000	2.0618333							
Corrected Total	19	274.0895000								

Source	DF	Type I SS	Mean Square	F Value	Pr > F
numpass	1	141.2953228	141.2953228	68.53	<.0001
cnumpass	3	101.8666772	33.9555591	16.47	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
numpass	0	0.0000000	.	.	.
cnumpass	3	101.8666772	33.9555591	16.47	<.0001

When t treatments have interval scale, the SLR model, and all polynomials of degree $p \leq t - 2$, are nested in one-factor ANOVA model with t treatment means.

F-ratio for lack-of-fit

To test for lack-of-fit of a polynomial (*reduced*) model of degree p , use extra sum-of-squares F-ratio on $t - 1 - p$ and $N - t$ *df*:

$$F = \frac{SS[\text{lack of fit}]/(t - 1 - p)}{MS[\text{pure error}]}, \quad \text{where}$$

$$MS[\text{pure error}] = MS[E]_{full} \quad \text{and}$$

$$\begin{aligned} SS[\text{lack-of-fit}] &= SS[Trt] - SS[R]_{poly} = SS[E]_{poly} - SS[E]_{full} \\ &= SS[E]_{poly} - SS[\text{pure error}] \end{aligned}$$

In a simple linear ($p = 1$) model for the meadows data,

$$SS[\text{lack of fit}] = 243.163 - 141.295 = 101.867 \quad \text{on} \quad t - 1 - p = 3df$$

and the sum of squares for pure error is $SS[E]_{full} = 30.93$ yielding

$$F = \frac{101.867/3}{30.93/15} \approx \frac{34}{2.1} = 16.5.$$

(highly significant since $F(0.01, 3, 15) = 5.42$.)

\Rightarrow model misspecified: SLR model suffers from lack of fit.

Some terminology for factorial experiments:

- contrasts
- orthogonal contrasts
- multiple contrasts
- expected mean squares
- familywise or experimentwise error rates
- power

Comparisons (contrasts) among means

Definition: In the one-way ANOVA layout:

$$Y_{ij} = \mu_i + E_{ij}, i = 1, 2, \dots, t, \text{ and } j = 1, 2, \dots, n_i$$

with $E_{ij} \stackrel{iid}{\sim} N(0, \sigma^2)$, A linear combination of treatment means, $\theta = \sum c_i \mu_i$ is called a _____ if .

$$c_1 + c_2 + \dots + c_t = \sum_{j=1}^t c_j = 0.$$

Definition: Contrasts in which only two of the coefficients are nonzero are called simple or _____ contrasts. Example: _____

Definition: Contrasts in with more than two nonzero coefficients are called _____ contrasts. Example: _____

Result: The *best* estimator for a contrast of interest obtained by substituting treatment group sample means \bar{y}_{i+} for treatment population means μ_i in the contrast θ :

$$\hat{\theta} = c_1 \bar{Y}_{1+} + c_2 \bar{Y}_{2+} + \dots + c_t \bar{Y}_{t+}.$$

For binding fractions, contrast penicillin and Tetracyclin (population) means

$$\theta = \mu_1 - \mu_2 = (1)\mu_1 + (-1)\mu_2 + (0)\mu_3 + (0)\mu_4 + (0)\mu_5$$

Using the result, point estimator of θ is

$$\hat{\theta} = \hat{\mu}_1 - \hat{\mu}_2 = \bar{Y}_{1+} - \bar{Y}_{2+}$$

Antibiotic	Binding Percentage				Sample mean	Sample variance
Penicillin G	29.6	24.3	28.5	32	28.6	10.4
Tetracyclin	27.3	32.6	30.8	34.8	31.4	10.1
Streptomycin	5.8	6.2	11	8.3	7.8	5.7
Erythromycin	21.6	17.4	18.3	19	19.1	3.3
Chloramphenicol	29.2	32.8	25	24.2	27.8	15.9

Source	d.f.	Sum of squares	Mean Square	F
Treatments	4	1481	370	41
Error	15	136	9.05	
Total	19	1617		

$$E\{MS(E)\} = \sigma^2$$

$$V(\bar{Y}_{1+}) = \frac{\sigma^2}{n_1}$$

Substitution of \bar{y}_{1+} and \bar{y}_{2+} yields $\hat{\theta} = 28.6 - 31.4 = -2.8$.

Q: How *good* is this estimate? (Quantify the associated uncertainty.)

Sampling distribution of $\hat{\theta}$

$\hat{\theta}$ a linear combo of independent averages of normals, hence normal with std.err.

$$SE(\hat{\theta}) = \sqrt{\frac{c_1^2}{n_1}\sigma^2 + \frac{c_2^2}{n_2}\sigma^2 + \dots + \frac{c_t^2}{n_t}\sigma^2} = \sqrt{\sigma^2 \sum_{i=1}^t \frac{c_i^2}{n_i}} = \sqrt{V(\sum c_i \bar{Y}_{i\cdot})}$$

estimated by

$$\hat{SE}(\hat{\theta}) = \sqrt{MS[E] \sum_{i=1}^t \frac{c_i^2}{n_i}} = \sqrt{\sum V(c_i \bar{Y}_{i\cdot}) + cov's}$$

$$= \sqrt{\sum c_i^2 \sigma^2 / n_i} \quad \phi$$

To test $H_0 : \theta = \theta_0$ (often 0) versus $H_1 : \theta \neq \theta_0$ a t use t -test:

$$t = \frac{\text{est} - \text{null}}{\hat{SE}} = \frac{\hat{\theta} - \theta_0}{\hat{SE}(\hat{\theta})} \stackrel{H_0}{\sim} t_{N-t}$$

At level α , the critical value for this test is $t(N - t, \alpha/2)$.

100(1 - α)% confidence interval for a contrast $\theta = \sum c_i \mu_i$ given by

$$\sum c_i \bar{Y}_{i\cdot} \pm t(\alpha/2, N - t) \sqrt{MS(E) \sum c_i^2 / n_i}$$

Here,

$$\widehat{SE}(\hat{\theta}) = \sqrt{\left(\frac{1^2}{n_1} + \frac{(-1)^2}{n_2}\right) (9.05)} = \sqrt{\frac{9.05}{2}} = 2.127$$

So that the t statistic becomes

$$\frac{\hat{\theta} - 0}{\widehat{SE}(\hat{\theta})} = \frac{-2.8}{2.127} = -1.32$$

which is not in the critical region, so that the sample mean binding fractions for Penicillin G and Tetracyclin do not differ significantly.

$$t_{0.025, 15} = 2.13$$

A 95% confidence interval is given by

$$-2.8 \pm 2.13(2.127) \text{ or } (-7.3, 1.7) \quad \exists 0 \rightarrow \text{plausible}$$

Code (next page) estimates all pairwise contrasts involving Pen. G:

$$\bullet \theta_1 = a'\mu = (1, -1, 0, 0, 0)\mu$$

$$\bullet \theta_2 = b'\mu = ? (1, 0, -1, 0, 0)\mu$$

$$\bullet \theta_3 = c'\mu = ? (1, 0, 0, -1, 0)\mu$$

$$\bullet \theta_4 = d'\mu = ? (1, 0, 0, 0, -1)\mu$$

along with complex contrast comparing Pen G. with mean of other four antibiotics:

$$\theta_5 = \left(1, -\frac{1}{4}, -\frac{1}{4}, -\frac{1}{4}, -\frac{1}{4}\right)\mu$$

Here $\mu = (\mu_1, \mu_2, \mu_3, \mu_4, \mu_5)'$.

```

proc glm data=one;
  class drug;
  model y=drug/clparm;
  estimate "theta1" drug 1 -1;
  estimate "theta2" drug 1 0 -1;
  estimate "theta3" drug 1 0 0 -1;
  estimate "theta4" drug 1 0 0 0 -1;
  estimate "theta5" drug 4 -1 -1 -1 -1/divisor=4;
run;

```

11000;

1 -0.25 -0.25 -0.25 -0.25

estimate "Pen6" drug 1;
NUE
estimate "Pen6" int 1
drug 1;

The GLM Procedure

Class Level Information

Class	Levels	Values
drug	5	1 2 3 4 5

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	1480.823000	370.205750	40.88	<.0001
Error	15	135.822500	9.054833		
Corrected Total	19	1616.645500			

R-Square	Coeff Var	Root MSE	y Mean
0.915985	13.12023	3.009125	22.93500

Source	DF	Type I SS	Mean Square	F Value	Pr > F
drug	4	1480.823000	370.205750	40.88	<.0001

Parameter	Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
theta1 PG - Tet →	-2.7750000	2.12777270	-1.30	0.2118	-7.3102402 1.7602402
theta2	20.7750000	2.12777270	9.76	<.0001	16.2397598 25.3102402
theta3	9.5250000	2.12777270	4.48	0.0004	4.9897598 14.0602402
theta4	0.8000000	2.12777270	0.38	0.7122	-3.7352402 5.3352402
theta5	7.0812500	1.68215202	4.21	0.0008	3.4958278 10.6666722

Pr all 5 intervals capture their θ_i targets $\leq .95$

Orthogonal contrasts: Let two contrasts θ_1 and θ_2 be given by

$$\theta_1 = c_1\mu_1 + \cdots + c_t\mu_t \quad \text{and} \quad \theta_2 = d_1\mu_1 + \cdots + d_t\mu_t$$

Definition: The two contrasts θ_1 and θ_2 are mutually orthogonal if the products of their coefficients sum to zero: $c_1d_1 + \cdots + c_t d_t = \sum_{i=1}^t c_i d_i = 0$. A set of several contrasts $\theta_1, \dots, \theta_k$ is mutually orthogonal if all pairs mutually orthogonal.

$$\begin{array}{lll} \hat{\theta}_1 \perp \hat{\theta}_2 & (-1, 1, 0, 0, 0) \text{ and } (0, 0, -1, 1, 0) \text{ orthogonal?} & \text{yes} \\ \hat{\theta}_3 \perp \hat{\theta}_4 & (1, -1/2, -1/2, 0, 0) \text{ and } (0, 0, 0, -1, 1) \text{ orthogonal?} & \text{yes} \\ \text{not indep} & (-1, \underline{1}, 0, 0, 0) \text{ and } (0, \underline{-1}, 1, 0, 0) \text{ orthogonal?} & \text{No} \end{array}$$

θ_i and θ_j orthogonal $\implies \hat{\theta}_i$ and $\hat{\theta}_j$ are statistically independent.

Contrast sums of squares

As $SS[Trt]$ quantifies treatment effect, $SS(\theta_i)$ quantifies contrast effect:

$$E(SS(\theta_i) | H_0: \theta_i = 0) = \sigma^2 \quad , \quad SS[\hat{\theta}_1] = \frac{\hat{\theta}_1^2}{\left(\frac{c_1^2}{n_1} + \dots + \frac{c_t^2}{n_t}\right)} = \frac{(\bar{y}_1 - \bar{y}_2)^2}{\frac{2}{4}}$$

If $\theta_1, \dots, \theta_{t-1}$ are $t - 1$ mutually orthogonal contrasts, then

$$SS[Trt] = SS(\hat{\theta}_1) + SS(\hat{\theta}_2) + \dots + SS(\hat{\theta}_{t-1})$$

For single df contrasts, if $H_0 : \theta_i = 0$,

$$E(SS[\hat{\theta}_j]) = \sigma^2.$$

To test $H_0 : \theta_j = 0$ versus $H_1 : \theta_j \neq 0$, use F below, with $df = \frac{1}{\sum_{i=1}^t (n_i - 1)} : \frac{N - t}{t(n - 1)}$:

$$F = \frac{SS[\hat{\theta}_j]}{MS[E]} = \frac{t^2}{H_0}$$

For $\theta_1 = \mu_1 - \mu_2$ in the binding fractions,

$$F = \frac{(-2.8)^2}{MS[E] \left(\frac{1}{4} + \frac{(-1)^2}{4} + 0 + 0 + 0 \right)} = 1.73.$$

$SS(\theta_1)$

(Using $F(0.05, 1, 15) = 4.54$, is $H_0 : \theta_1 = 0$ plausible?)

Number of contaminants in IV fluids made by $t = 3$ pharmaceutical companies

Nancy's

Chicago

$$MS(E) = \frac{1}{3} (S_C^2 + S_A^2 + S_M^2)$$

$$MS(Trt) = \frac{1}{3-1} \sum_{i=1}^3 \sum_{j=1}^6 (Y_{ij} - \bar{Y}_{i.})^2$$

	Cutter	Abbott	McGaw
	255	105	577
	264	288	515
	342	98	214
	331	275	413
	234	221	401
	217	240	260
\bar{y}_{i+}	273.8	204.5	396.7

$$Y_{ij} = \mu + \tau_i + \epsilon_{ij}$$

↑
 $N(0, \sigma^2)$

Source	d.f.	Sum of squares	Mean Square	F
Treatments (or pharmacies)	2	113646	56823	5.8
Error	15	146753	9784	
Total	17	260400		

Consider the following 2 contrasts:

$$H_0: \tau_1 = \tau_2 = \tau_3 = 0$$

$$\theta_1 = \mu_M - \mu_A \quad \text{and} \quad \theta_2 = \mu_C - \frac{\mu_M + \mu_A}{2}$$

$$\theta_1 = (0, -1, 1) \mu$$

$$\theta_2 = (1, -\frac{1}{2}, -\frac{1}{2}) \mu$$

Q: Are these contrasts orthogonal? *yes*

Q: Are the estimated contrasts $\hat{\theta}_1$ and $\hat{\theta}_2$ independent?

Exercise: Compute $SS[\hat{\theta}_1]$ and $SS[\hat{\theta}_2]$. Add em up.

yes

```

proc glm order=formatted;
  title "contaminant particles in IV fluids";
  class firm;
  model con=firm;
  contrast 'C - avg of M and A' firm -0.5 1 -0.5;
  contrast 'McGaw - Abbott' firm -1 0 1;
  estimate 'C - avg of M and A' firm -0.5 1 -0.5;
  estimate 'McGaw - Abbott' firm -1 0 1;
run;

```

contaminant particles in IV fluids 1
The GLM Procedure

Class	Levels	Values
firm	3	Abbott Cutter McGaw

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	2	113646.3333	56823.1667	5.81	0.0136
Error	15	146753.6667	9783.5778		
Corrected Total	17	260400.0000			

R-Square	Coeff Var	Root MSE	con Mean
0.436430	33.91268	98.91197	291.6667

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
C - avg of M and A	1	2862.2500	2862.2500	0.29	0.5965
McGaw - Abbott	1	110784.0833	110784.0833	11.32	0.0043

Parameter	Estimate	Standard Error	t Value	Pr > t
C - avg of M and A	-26.750000	49.4559849	-0.54	0.5965
McGaw - Abbott	192.166667	57.1068524	3.37	0.0043

$$\frac{(192)^2}{2/6}$$

Multiple Comparisons

- Too many tests of significance brings creeping type I error rate
- e.g. consider the case with $t = 5$ (antibiotic treatments): all simple (pairwise) contrasts of the form $\theta = \mu_i - \mu_j$
- $\binom{5}{2} = 10$ tests of significance each at level $\alpha = 0.05$

$$H_0: \theta_1 = 0 \quad H_0: \theta_2 = 0 \quad \dots \quad H_0: \theta_{10} = 0$$

When testing k contrasts, the experimentwise error rate (or familywise) is

$$\geq fwe = \Pr(\text{at least one type I error})$$

Methods for simultaneous inference for multiple contrasts include

- Bonferroni
- Tukey
- Scheffé (won't cover)

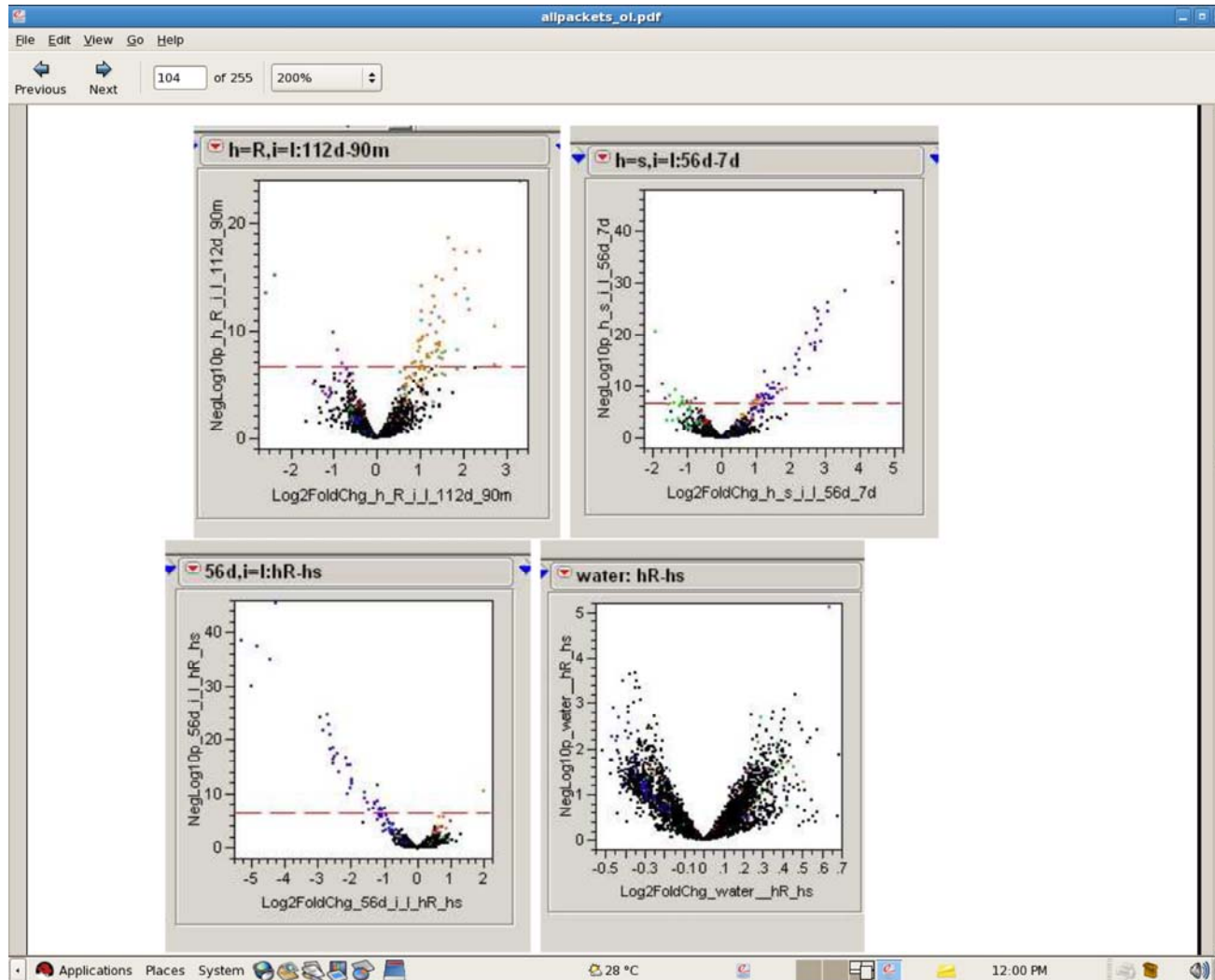
When the number of comparisons is in the thousands, and FWE control is hopeless, more manageable type I error rate is the False Discovery Rate (**FDR**):

$$FDR = E \left(\frac{\text{Falsely rejected null hypotheses}}{\text{Number of rejected null hypotheses}} \right)$$

See `qvalue()` in R and

<http://www4.stat.ncsu.edu/~jaosborn/research/microarray/software/qvalues.sas>

A context in which multiplicity is a big issue:
Microarray experiments, which may involve thousands of genes and tests



(Data courtesy of Cassi Myburg)

Bonferroni

Consider k contrasts of interest. Bonferroni adjustment to α which controls fwe is

$$\alpha' = \frac{\alpha}{k}$$

Simultaneous 95% confidence intervals for the k contrasts given by

$$a_1 \bar{Y}_{1+} + a_2 \bar{Y}_{2+} + \cdots + a_t \bar{Y}_{t+} \pm t\left(\frac{\alpha'}{2}, \nu\right) \sqrt{MS[E] \sum \frac{a_j^2}{n_j}}$$

and

$$b_1 \bar{Y}_{1+} + b_2 \bar{Y}_{2+} + \cdots + b_t \bar{Y}_{t+} \pm t\left(\frac{\alpha'}{2}, \nu\right) \sqrt{MS[E] \sum \frac{b_j^2}{n_j}}$$

\vdots

$$k_1 \bar{Y}_{1+} + k_2 \bar{Y}_{2+} + \cdots + k_t \bar{Y}_{t+} \pm t\left(\frac{\alpha'}{2}, \nu\right) \sqrt{MS[E] \sum \frac{k_j^2}{n_j}}$$

where ν denotes df for error. $t(\frac{\alpha'}{2}, \nu)$ might have to be obtained using software.

For the binding fraction example, consider only pairwise comparisons with Penicillin:

$$\theta_1 = \mu_1 - \mu_2, \theta_2 = \mu_1 - \mu_3, \theta_3 = \mu_1 - \mu_4, \theta_4 = \mu_1 - \mu_5$$

We have $k = 4$, $\alpha' = 0.05/k = 0.0125$, and $t(\frac{\alpha'}{2}, 15) = \underline{\hspace{2cm}}$.

Substitution leads to

$$t(\alpha', 15) \sqrt{MS[E] \left(\frac{(-1)^2}{4} + \frac{(-1)^2}{4} + \frac{0^2}{4} + \cdots \frac{0^2}{4} \right)} = 2.84 \sqrt{(9.05) \frac{2}{4}} = 6.0$$

so that simultaneous 95% confidence intervals for $\theta_1, \theta_2, \theta_3, \theta_4$ take the form

$$\bar{y}_1 - \bar{y}_i \pm 6.0$$

```
proc glm data=one;      *In SAS, adjustment for k=4 achieved with care;
  title "Bonferroni correction for 4 contrasts";
  class drug;
  model y=drug/clparm alpha=.0125;
  estimate "theta1" drug -1 1;
  estimate "theta2" drug -1 0 1;
  estimate "theta3" drug -1 0 0 1;
  estimate "theta4" drug -1 0 0 0 1;
run;
```

Bonferroni correction for 4 contrasts
The GLM Procedure

Parameter	Estimate	Standard Error	t Value	Pr > t	98.75% Confidence Limits	
theta1	2.7750000	2.12777270	1.30	0.2118	-3.2606985	8.8106985
theta2	-20.7750000	2.12777270	-9.76	<.0001	-26.8106985	-14.7393015
theta3	-9.5250000	2.12777270	-4.48	0.0004	-15.5606985	-3.4893015
theta4	-0.8000000	2.12777270	-0.38	0.7122	-6.8356985	5.2356985

(actually simultaneous **95%** confidence intervals)

Tukey

Tukey's method better than Scheffé's method for all pairwise comparisons in balanced designs is conservative, controlling experimentwise error rate, and has lower type II error rate in these cases than Scheffé. (More powerful.)

For simple contrasts of the form

$$\theta = \mu_j - \mu_k$$

to test

$$H_0 : \theta = 0 \text{ vs } H_1 : \theta \neq 0$$

reject H_0 at level α if

$$|\hat{\theta}| > q(t, N - t, \alpha) \sqrt{\frac{MS[E]}{n}}$$

where $q(t, N - t, \alpha)$ denotes α level *studentized range* for t means and $N - t$ degrees of freedom. These studentized ranges can be found in Table C.11 of Rao.

For the IV data, $q(3, 15, 0.05) = 3.67$. Tukey's 95% honestly significant difference (HSD) for pairwise comparisons of treatment means in this balanced design are

$$3.67 \sqrt{\frac{MS(E)}{n}} = \underline{\hspace{2cm}} = \underline{\hspace{2cm}}$$

```

proc glm;
  class firm;
  model con=firm;
  means firm/scheffe tukey;
run;

```

Tukey's Studentized Range (HSD) Test for con

NOTE: This test controls the Type I experimentwise error rate, but it generally has a higher Type II error rate than REGWQ.

Alpha	0.05
Error Degrees of Freedom	15
Error Mean Square	9783.578
Critical Value of Studentized Range	3.67338
Minimum Significant Difference	148.33

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	firm
A	396.67	6	McGaw
B A	273.83	6	Cutter
B	204.50	6	Abbott

(Scheffé excluded)

Expected mean squares

Definition: The treatment mean square is given by

$$MS[Trt] = \frac{SS[Trt]}{t-1} = \frac{1}{t-1} \sum_i \sum_j (\bar{y}_{i+} - \bar{y}_{..})^2$$

$$(\bar{y}_{..} = \bar{y}_{++} \text{ and } \bar{y}_{i+} = \frac{1}{n_i} \sum_{j=1}^{n_i} y_{ij})$$

$$\begin{aligned} E[MS[Trt]; H_1] &= E[SS[Trt]/(t-1); H_1] \\ &= \sigma^2 + \frac{1}{t-1} \sum n_i (\mu_i - \mu)^2 \\ &= \sigma^2 + n \frac{1}{t-1} \sum (\mu_i - \mu)^2 \text{ (balanced case)} \\ &= \sigma^2 + n\psi_T^2 \end{aligned}$$

$$\text{where } \psi_T^2 = \frac{1}{t-1} \sum (\mu_i - \mu)^2.$$

Note that under $H_0 : \mu_i \equiv \mu$ and $\psi_T^2 = 0$ so that

$$E[MS[Trt]; H_0] = E[SS[Trt]/(t-1); H_0] = \underline{\hspace{2cm}}$$

$MS[E] = \frac{SS[E]}{N-t}$, (generalization of pooled variance S_p^2 to $t > 2$ groups):

$$\begin{aligned} MS[E] &= \frac{SS[E]}{N-t} = \frac{1}{N-t} \sum_{i=1}^{i=t} \sum_{j=1}^{j=n_i} (y_{ij} - \bar{y}_{i+})^2 \\ &= \frac{1}{N-t} \sum_{i=1}^t (n_i - 1) s_i^2 \\ &= \left(\frac{n_1 - 1}{N-t} \right) s_1^2 + \left(\frac{n_2 - 1}{N-t} \right) s_2^2 + \cdots + \left(\frac{n_t - 1}{N-t} \right) s_t^2 \\ &= "S_p^2" \end{aligned}$$

Since $E(S_i^2) = \sigma^2$, $MS[E]$ is unbiased for σ^2 regardless of H_0 or H_1 :

$$\begin{aligned} E(S_i^2) &= \sigma^2 \implies \\ E[MS[E]] &= \left(\frac{n_1 - 1}{N-t} \right) \sigma^2 + \left(\frac{n_2 - 1}{N-t} \right) \sigma^2 + \cdots + \left(\frac{n_t - 1}{N-t} \right) \sigma^2 \\ &= \sigma^2 \end{aligned}$$

$$E[MS[E]] = \sigma^2$$

Sample size computations for one-way ANOVA

Consider designing a completely randomized experiment that will have significance level α , power $1 - \beta$, and sample size n to accept or reject the following hypotheses regarding the means of a response variable, Y with error variance σ^2 :

$$H_0 : \mu_1 = \cdots = \mu_t \quad \text{vs} \quad H_a : \psi_T^2 = \frac{1}{t-1} \sum (\mu_i - \mu)^2.$$

Linear model, i.i.d. normal errors \rightarrow can calculate any one quantity given others.

With H_0 true, $F = MS(Trt)/MS(E)$ follows an F-distribution under

With H_a true, $F = MS(Trt)/MS(E)$ follows a non-central F-distribution with non-centrality parameter given below ($\tau_i = \mu_i - \bar{\mu}$):

$$\gamma =$$

- Suppose $t = 4$, $n = 9$ ($N = 36$), $\sigma^2 = 9$, $\alpha = .05$ and the hypotheses are

$$H_0 : \mu_1 = \cdots = \mu_4 \quad \text{vs} \quad H_a : \mu_1 = \mu_2 = 9, \mu_3 = 10, \mu_4 = 12.$$

Calculate the power, $P(\text{reject } H_0 | H_a \text{ true})$. (an area under non-central F density).

```
> my.ncp <- 9*3*var(c(9,9,10,12))/9
> 1-pf(qf(.95,3,32),3,32,my.ncp)
[1] 0.4655894
```

Another example: consider these hypotheses for antibiotic binding fractions:

$$H_1 : \mu_P = \mu + 3, \mu_T = \mu + 3, \mu_S = \mu - 6, \mu_E = \mu, \mu_C = \mu$$

Assume $\sigma = 3$ and we need to use $\alpha = \beta = 0.05$.

$$\gamma = n\left[\left(\frac{3}{3}\right)^2 + \left(\frac{3}{3}\right)^2 + \left(\frac{-6}{3}\right)^2\right].$$

The following code should do the trick to calculate the necessary n

```
data one;
  do n=2 to 10;
    t=5; nu1=t-1; nu2=t*(n-1);
    sumtau2=3**2+3**2+(-6)**2;
    sigma2=9;
    ncp=n*sumtau2/sigma2;
    qf=finv(0.95,nu1,nu2);
    pf=probf(qf,nu1,nu2,ncp);
    power=1-pf;
    output;
  end;
run;
proc print;run;
```

OBS	N	T	NU1	NU2	SUMTAU2	SIGMA2	NCP	QF	PF	POWER
1	2	5	4	5	54	9	12	5.19217	0.59246	0.40754
2	3	5	4	10	54	9	18	3.47805	0.22465	0.77535
3	4	5	4	15	54	9	24	3.05557	0.06437	0.93563
4	5	5	4	20	54	9	30	2.86608	0.01533	0.98467
5	6	5	4	25	54	9	36	2.75871	0.00319	0.99681
6	7	5	4	30	54	9	42	2.68963	0.00060	0.99940

(not needed)