# Chapter 14 Weighted Least Squares

## 14.1 Introduction

- Previous chapters discussed logistic regression models using maximum likelihood estimation
- Functions modeled were logits, or cumulative logits
- What about modeling other functions of categorical data? Might be interested in mean scores, proportions, or more complicated functions of responses
- Weighted least squares provides methodology for wide range of functions. This chapter focuses on mean scores and proportions, as well as estimates from complex sample survey designs

- CATMOD is a general procedure used for modeling categorical data:

    1) For response function = **generalized logits**, CATMOD performs **logistic regression** using **maximum likelihood estimation**

    2) For response function = **means, etc.,** CATMOD performs **weighted least squares** analysis

# Statistical Methodology for Weighted Least Squares

| Group | Response | | | | Total |
|---|---|---|---|---|---|
| | 1 | 2 | . . . | $r$ | |
| 1 | $n_{11}$ | $n_{12}$ | . . . | $n_{1r}$ | $n_{1+}$ |
| 2 | $n_{21}$ | $n_{22}$ | . . . | $n_{2r}$ | $n_{2+}$ |
| . | . | . | . | . | . |
| . | . | . | . | . | . |
| . | . | . | . | . | . |
| $s$ | $n_{s1}$ | $n_{s2}$ | . . . | $n_{sr}$ | $n_{s+}$ |

Proportion of subjects in $i^{\text{th}}$ group who have $j^{\text{th}}$ response is

$$p_{ij} = n_{ij} / n_{i+}$$

Suppose $\boldsymbol{n}_i' = (n_{i1}, n_{i2}, ..., n_{ir})$ represents vector of responses for $i^{\text{th}}$ subpopulation, and $\boldsymbol{n}' = (\boldsymbol{n}_1', \boldsymbol{n}_2', ..., \boldsymbol{n}_s')$, then $\boldsymbol{n}$ follows product multinomial distribution:

$$\Pr\{\boldsymbol{n}\} = \prod_{i=1}^{s} n_{i+}! \prod_{j=1}^{r} \pi_{ij}^{n_{ij}} / n_{ij}!,$$

where $\pi_{ij}$ is probability that a randomly selected subject from $i^{\text{th}}$ group has $j^{\text{th}}$ response profile. The $\pi_{ij}$ satisfy the natural restrictions

$$\sum_{j=1}^{r} \pi_{ij} = 1 \text{ for } i = 1, 2, ..., s.$$

Suppose $\boldsymbol{p}_i = \boldsymbol{n}_i / n_{i+}$ is $r \times 1$ vector of observed proportions for $i$th group, and $\boldsymbol{p}' = (\boldsymbol{p}_1', \boldsymbol{p}_2', ..., \boldsymbol{p}_s')$ is $(sr \times 1)$ compound vector of proportions. Then a consistent estimator of covariance matrix for proportions in $i$th row is:

$$\boldsymbol{V}(\boldsymbol{p}_i) = \frac{1}{n_{i+}} \begin{bmatrix} p_{i1}(1-p_{i1}) & -p_{i1}p_{i2} & \cdots & -p_{i1}p_{ir} \\ -p_{i2}p_{i1} & p_{i2}(1-p_{i2}) & \cdots & -p_{i2}p_{ir} \\ \vdots & \vdots & \ddots & \vdots \\ -p_{ir}p_{i1} & -p_{ir}p_{i2} & \cdots & p_{ir}(1-p_{ir}) \end{bmatrix}$$

and covariance matrix for vector $\boldsymbol{p}$ is:

$$\boldsymbol{V}_{\boldsymbol{p}} = \begin{bmatrix} \boldsymbol{V}_1 & \boldsymbol{0} & \cdots & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{V}_2 & \cdots & \boldsymbol{0} \\ \vdots & \vdots & \ddots & \vdots \\ \boldsymbol{0} & \boldsymbol{0} & \cdots & \boldsymbol{V}_s \end{bmatrix}$$

where $\boldsymbol{V}_i$ is covariance matrix for $\boldsymbol{p}_i$ .

Suppose $\boldsymbol{F}_1(\boldsymbol{p})$, $\boldsymbol{F}_2(\boldsymbol{p})$, …, $\boldsymbol{F}_u(\boldsymbol{p})$ is a set of $u$ functions of $\boldsymbol{p}$. Each is required to have continuous partial derivatives through order two, and $\boldsymbol{F}$ must have nonsingular covariance matrix:

$$\boldsymbol{V}_F(\boldsymbol{\pi}) = \left[\boldsymbol{H}(\boldsymbol{\pi})\right]\left[\boldsymbol{V}(\boldsymbol{\pi})\right]\left[\boldsymbol{H}(\boldsymbol{\pi})\right]',$$

where $\boldsymbol{H}(\boldsymbol{\pi}) = \left[\left.\frac{\partial \boldsymbol{F}}{\partial \boldsymbol{z}}\right|_{\boldsymbol{z}=\boldsymbol{\pi}}\right]$ is the first derivative matrix of $\boldsymbol{F}(\boldsymbol{z})$.

$\boldsymbol{F}$ is consistent estimator of $\boldsymbol{F}(\boldsymbol{\pi})$, so linear model can be used to investigate variability among elements of $\boldsymbol{F}(\boldsymbol{\pi})$:

$$\boldsymbol{E}_{\boldsymbol{A}}\{\boldsymbol{F}(\boldsymbol{p})\} = \boldsymbol{F}(\boldsymbol{\pi}) = \boldsymbol{X}\boldsymbol{\beta},$$

where $\boldsymbol{X}$ is known model matrix with rank $t \leq u$, $\boldsymbol{\beta}$ is $t \times 1$ vector of unknown parameters.

Goodness of fit of model is assessed with

$$Q(\boldsymbol{X},\boldsymbol{F}) = (\boldsymbol{W}\boldsymbol{F})' \, [\boldsymbol{W}\boldsymbol{V}_{\boldsymbol{F}}\boldsymbol{W}']^{-1}\boldsymbol{W}\boldsymbol{F},$$

where $\boldsymbol{W}$ is any fullrank $[(u - t) \times u]$ matrix orthogonal to $\boldsymbol{X}$. $Q(\boldsymbol{X},\boldsymbol{F})$ is approximately distributed chi-square with $(u - t)$ degrees of freedom when sample sizes large enough so that elements of $\boldsymbol{F}$ have approximate multivariate normal distribution. (Wald statistics).

The following statistic

$$Q_W = (\boldsymbol{F} - \boldsymbol{X}\boldsymbol{b})'\boldsymbol{V}_F^{-1}(\boldsymbol{F} - \boldsymbol{X}\boldsymbol{b})$$

is identical to $Q(\boldsymbol{X},\boldsymbol{F})$ and obtained by using weighted least squares to produce estimate for $\boldsymbol{\beta}$.

$$\boldsymbol{b} = (\boldsymbol{X}'\boldsymbol{V}_F^{-1}\boldsymbol{X})^{-1}\boldsymbol{X}'\boldsymbol{V}_F^{-1}\boldsymbol{F}$$

which is minimum modified chi-square estimator.

Consistent estimator for covariance matrix of $\boldsymbol{b}$ is

$$\boldsymbol{V}(\boldsymbol{b}) = (\boldsymbol{X}'\boldsymbol{V}_F^{-1}\boldsymbol{X})^{-1}.$$

Linear hypotheses of form $\boldsymbol{C\beta} = \mathbf{0}$, where $\boldsymbol{C}$ is known $c \times t$ matrix of constants of rank $c$, can be tested with Wald statistic

$$Q_C = (\boldsymbol{Cb})' \left[ \boldsymbol{C}(\boldsymbol{X}'\boldsymbol{V}_{\boldsymbol{F}}^{-1}\boldsymbol{X})^{-1}\boldsymbol{C}' \right]^{-1} (\boldsymbol{Cb})$$

$Q_C$ is distributed chi-square with $c$ degrees of freedom.

Predicted values for $\boldsymbol{F}(\boldsymbol{\pi})$ can be calculated from

$$\hat{\boldsymbol{F}} = \boldsymbol{Xb} = \boldsymbol{X}(\boldsymbol{X}'\boldsymbol{V}_{\boldsymbol{F}}^{-1}\boldsymbol{X})^{-1}\boldsymbol{X}'\boldsymbol{V}_{\boldsymbol{F}}^{-1}\boldsymbol{F}$$

and consistent estimators for variances of $\hat{\boldsymbol{F}}$ can be obtained from diagonal elements of

$$\boldsymbol{V}_{\hat{\boldsymbol{F}}} = \boldsymbol{X}(\boldsymbol{X}'\boldsymbol{V}_{\boldsymbol{F}}^{-1}\boldsymbol{X})^{-1}\boldsymbol{X}'.$$

While $\boldsymbol{F}(\boldsymbol{p})$ can take on wide range of forms, a few functions are commonly used. You can fit a strictly linear model

$$\boldsymbol{F}(\boldsymbol{p}) = \boldsymbol{A}\boldsymbol{p},$$

where $\boldsymbol{A}$ is matrix for known constants. Covariance matrix of $\boldsymbol{F}$ is written

$$\boldsymbol{V}_{\boldsymbol{F}} = \boldsymbol{A}\boldsymbol{V}_{\boldsymbol{p}}\boldsymbol{A}'.$$

Another common model is loglinear:

$$\boldsymbol{F}(\boldsymbol{p}) = \boldsymbol{A} \log \boldsymbol{p},$$

where log transforms vector to corresponding vector of natural logarithms and $\boldsymbol{A}$ is orthogonal to $\mathbf{1}$ (vector of 1's). In this case,

$$\boldsymbol{V}_{\boldsymbol{F}} = \boldsymbol{A}\boldsymbol{D}_{\boldsymbol{p}}^{-1}\boldsymbol{A}'$$

Where $\boldsymbol{D}_{\boldsymbol{p}}$ is diagonal matrix with elements of $\boldsymbol{p}$ on diagonal.

Many other useful functions can be generated as a sequence of linear, logarithmic, and exponential operations on vector $\boldsymbol{p}$.

- linear transformations: $\boldsymbol{F}_1(\boldsymbol{p}) = \boldsymbol{A}_1\boldsymbol{p} = \boldsymbol{\alpha}_1$
- logarithmic: $\boldsymbol{F}_2(\boldsymbol{p}) = \log(\boldsymbol{p}) = \boldsymbol{\alpha}_2$
- exponential: $\boldsymbol{F}_3(\boldsymbol{p}) = \exp(\boldsymbol{p}) = \boldsymbol{\alpha}_3$

Corresponding $\boldsymbol{H}_k$ matrix operators needed to produce covariance matrix for $F$ are

- $\boldsymbol{H}_1 = \boldsymbol{A}_1$
- $\boldsymbol{H}_2 = \boldsymbol{D}_{\boldsymbol{p}}^{-1}$
- $\boldsymbol{H}_3 = \boldsymbol{D}_{\alpha 3}$

$\boldsymbol{V}_{\boldsymbol{F}}$ is estimated by $\boldsymbol{V}_{\boldsymbol{F}} = [\boldsymbol{H}(\boldsymbol{p})]\boldsymbol{V}_{\boldsymbol{p}}[\boldsymbol{H}(\boldsymbol{p})]'$ where $\boldsymbol{H}(\boldsymbol{p})$ is a product of first derivative matrices $\boldsymbol{H}_k(\boldsymbol{p})$ where $k$ indicates $i$th operation in accordance with chain rule.

## 14.2 Weighted Least Squares Methodology

- The following example is used to motivate this discussion:

  Epidemiologists investigating air pollution effects conducted a study of childhood respiratory disease. Investigators interested in determining whether sex or residence affected the distribution of colds.

Periods with colds

| Sex | Res | 0 | 1 | 2 | Total |
|---|---|---|---|---|---|
| Female | Rural | 45 | 64 | 71 | 180 |
| Female | Urban | 80 | 104 | 116 | 300 |
| Male | Rural | 84 | 124 | 82 | 290 |
| Male | Urban | 106 | 117 | 87 | 310 |

- Chapter 9 would suggest using proportional odds model, but response measure of interest is mean number of periods with colds

- Due to small, discrete number of response values, assumptions of standard linear model are unlikely to be met

- With only assumption of sufficient sample size ( $\approx$ 30 per group), weighted least squares provides useful strategy for analyzing data

To compute the mean periods of colds for females in a rural residence:

$$\begin{aligned}\text{mean colds} &= 0\times p_{11} + 1\times p_{12} + 2\times p_{13} \\ &= 0\times(0.25) + 1\times(0.36) + 2\times(0.39) \\ &= 1.14\end{aligned}$$

In matrix formulation, this is written

$$\boldsymbol{A}\boldsymbol{p}_1 = \begin{bmatrix} 0 & 1 & 2 \end{bmatrix} \boldsymbol{p}_1 = \begin{bmatrix} 0 & 1 & 2 \end{bmatrix} \begin{bmatrix} 0.25 \\ 0.36 \\ 0.39 \end{bmatrix} = 1.14$$

The response functions for all of the colds data are

$$\boldsymbol{F}(\boldsymbol{p}) = \boldsymbol{A}\boldsymbol{p} = \begin{bmatrix} 1.14 \\ 1.12 \\ 0.99 \\ 0.94 \end{bmatrix}$$

Now fit a statistical model that determines the effect of sex and residence on the mean functions.

$$\begin{bmatrix} \boldsymbol{F}(\boldsymbol{p}_1) \\ \boldsymbol{F}(\boldsymbol{p}_2) \\ \boldsymbol{F}(\boldsymbol{p}_3) \\ \boldsymbol{F}(\boldsymbol{p}_4) \end{bmatrix} = \begin{bmatrix} \alpha + \beta_1 + \beta_2 + \beta_3 \\ \alpha + \beta_1 - \beta_2 - \beta_3 \\ \alpha - \beta_1 + \beta_2 - \beta_3 \\ \alpha - \beta_1 - \beta_2 + \beta_3 \end{bmatrix}$$

$$= \begin{bmatrix} 1 & 1 & 1 & 1 \\ 1 & 1 & -1 & -1 \\ 1 & -1 & 1 & -1 \\ 1 & -1 & -1 & 1 \end{bmatrix} \begin{bmatrix} \alpha \\ \beta_1 \\ \beta_2 \\ \beta_3 \end{bmatrix}$$

- $\alpha$ is the intercept
- $\beta_1$ is the differential effect for gender
- $\beta_2$ is the differential effect for residence
- $\beta_3$ represents their interaction

- The intercept is the mean number of colds averaged equally over all the groups.

- The differential effects represent deviations from the mean, so this model is known as a *deviation from the mean* model.

- The CATMOD procedure uses *fullrank* parameterization. If an effect such as gender or residence has *r* levels, then it is represented by *r* – 1 parameters.

## 14.3 Using PROC CATMOD for Weighted Least Squares Analysis

The following statements create SAS data set COLDS.

```
data colds;
   input sex $ residence $ periods count @@;
   datalines;
female rural 0 45 female rural 1 64  female rural 2 71
female urban 0 80 female urban 1 104 female urban 2 116
male rural   0 84 male   rural 1 124 male   rural 2 82
male urban   0 106 male  urban 1 117 male   urban 2 87
;
run;
```

The following set of SAS statements requests that a weighted least squares analysis be performed for the mean response, using the saturated model.

```
proc catmod;
   weight count;
   response means;
   model periods = sex residence sex*residence
                                   /freq prob design;
run;
```

- one mean function computed per group
- WLS is the default estimation method for functions other than logits (maximum likelihood for logits)
- WEIGHT statement required for frequency from data

## **Output 14.1** Population and Response Profiles

POPULATION PROFILES

| Sample | SEX | RESIDNCE | Sample Size |
|---|---|---|---|
| 1 | female | rural | 180 |
| 2 | female | urban | 300 |
| 3 | male | rural | 290 |
| 4 | male | urban | 310 |

RESPONSE PROFILES

| Response | PERIODS |
|---|---|
| 1 | 0 |
| 2 | 1 |
| 3 | 2 |

## **Output 14.2** Table Frequencies and Proportions

RESPONSE FREQUENCIES

| Sample | Response Number 1 | 2 | 3 |
|---|---|---|---|
| 1 | 45 | 64 | 71 |
| 2 | 80 | 104 | 116 |
| 3 | 84 | 124 | 82 |
| 4 | 106 | 117 | 87 |

RESPONSE PROBABILITIES

| Sample | Response Number 1 | 2 | 3 |
|---|---|---|---|
| 1 | 0.25 | 0.35556 | 0.39444 |
| 2 | 0.26667 | 0.34667 | 0.38667 |
| 3 | 0.28966 | 0.42759 | 0.28276 |
| 4 | 0.34194 | 0.37742 | 0.28065 |

**Output 14.3** Observed Response Functions and Model Matrix

| Sample | Response Function | DESIGN MATRIX 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| 1 | 1.14444 | 1 | 1 | 1 | 1 |
| 2 | 1.12000 | 1 | 1 | -1 | -1 |
| 3 | 0.99310 | 1 | -1 | 1 | -1 |
| 4 | 0.93871 | 1 | -1 | -1 | 1 |

**Output 14.4** ANOVA Table

ANALYSIS-OF-VARIANCE TABLE

| Source | DF | Chi-Square | Prob |
|---|---|---|---|
| INTERCEPT | 1 | 1841.13 | <.0001 |
| SEX | 1 | 11.57 | 0.0007 |
| RESIDNCE | 1 | 0.65 | 0.4202 |
| SEX*RESIDNCE | 1 | 0.09 | 0.7594 |
| RESIDUAL | 0 | . | . |

The main effects model is specified.

```
proc catmod;
   weight count;
   response means ;
   model periods = sex residence ;
run;
```

ANALYSIS-OF-VARIANCE TABLE

| Source | DF | Chi-Square | Prob |
|---|---|---|---|
| INTERCEPT | 1 | 1882.77 | <.0001 |
| SEX | 1 | 12.08 | 0.0005 |
| RESIDNCE | 1 | 0.76 | 0.3839 |
| RESIDUAL | 1 | 0.09 | 0.7594 |

The following code requests the single main effect model.

```
proc catmod;
   population sex residence;
   weight count;
   response means;
   model periods = sex;
run;
```

ANALYSIS-OF-VARIANCE TABLE

| Source | DF | Chi-Square | Prob |
|---|---|---|---|
| INTERCEPT | 1 | 1899.55 | <.0001 |
| SEX | 1 | 11.53 | 0.0007 |
| RESIDUAL | 2 | 0.85 | 0.6531 |

# 14.4 Obstetrical Pain Data: Advanced Modeling of Means

Table 14.4 Number of Hours with Little or No Pain for Women Who Recently Delivered a Baby

| Initial Pain | | | Hours With Little or No Pain | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Center | Status | Treatment | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Total |
| 1 | lot | placebo | 6 | 1 | 2 | 2 | 2 | 3 | 7 | 3 | 0 | 26 |
| 1 | lot | a | 6 | 3 | 1 | 2 | 4 | 4 | 7 | 1 | 0 | 28 |
| 1 | lot | b | 3 | 1 | 0 | 4 | 2 | 3 | 11 | 4 | 0 | 28 |
| 1 | lot | ba | 0 | 0 | 0 | 1 | 1 | 7 | 9 | 6 | 2 | 26 |
| 1 | some | placebo | 1 | 0 | 3 | 0 | 2 | 2 | 4 | 4 | 2 | 18 |
| 1 | some | a | 2 | 1 | 0 | 2 | 1 | 2 | 4 | 5 | 1 | 18 |
| 1 | some | b | 0 | 0 | 0 | 1 | 0 | 3 | 7 | 6 | 2 | 19 |
| 1 | some | ba | 0 | 0 | 0 | 0 | 1 | 3 | 5 | 4 | 6 | 19 |
| 2 | lot | placebo | 7 | 2 | 3 | 2 | 3 | 2 | 3 | 2 | 2 | 26 |
| 2 | lot | a | 3 | 1 | 0 | 0 | 3 | 2 | 9 | 7 | 1 | 26 |
| 2 | lot | b | 0 | 0 | 0 | 1 | 1 | 5 | 8 | 7 | 4 | 26 |
| 2 | lot | ba | 0 | 1 | 0 | 0 | 1 | 2 | 8 | 9 | 5 | 26 |
| 2 | some | placebo | 2 | 0 | 2 | 1 | 3 | 1 | 2 | 5 | 4 | 20 |
| 2 | some | a | 0 | 0 | 0 | 1 | 1 | 1 | 8 | 1 | 7 | 19 |
| 2 | some | b | 0 | 2 | 0 | 1 | 0 | 1 | 4 | 6 | 6 | 20 |
| 2 | some | ba | 0 | 0 | 0 | 1 | 3 | 0 | 4 | 7 | 5 | 20 |

## Table 14.4 Continued

| Initial Pain | | | Hours With Little or No Pain | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Center | Status | Treatment | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Total |
| 3 | lot | placebo | 6 | 0 | 2 | 2 | 2 | 6 | 1 | 2 | 1 | 22 |
| 3 | lot | a | 4 | 2 | 1 | 5 | 1 | 1 | 3 | 2 | 3 | 22 |
| 3 | lot | b | 5 | 0 | 2 | 3 | 1 | 0 | 2 | 6 | 7 | 26 |
| 3 | lot | ba | 3 | 2 | 1 | 0 | 0 | 2 | 5 | 9 | 4 | 26 |
| 3 | some | placebo | 5 | 0 | 0 | 1 | 3 | 1 | 4 | 4 | 5 | 23 |
| 3 | some | a | 1 | 0 | 0 | 1 | 3 | 5 | 3 | 3 | 6 | 22 |
| 3 | some | b | 3 | 0 | 1 | 1 | 0 | 0 | 3 | 7 | 11 | 26 |
| 3 | some | ba | 0 | 0 | 0 | 1 | 1 | 4 | 2 | 4 | 13 | 25 |
| 4 | lot | placebo | 4 | 0 | 1 | 3 | 2 | 1 | 1 | 2 | 2 | 16 |
| 4 | lot | a | 0 | 1 | 3 | 1 | 1 | 6 | 1 | 3 | 6 | 22 |
| 4 | lot | b | 0 | 0 | 0 | 0 | 2 | 7 | 2 | 2 | 9 | 22 |
| 4 | lot | ba | 1 | 0 | 3 | 0 | 1 | 2 | 3 | 4 | 8 | 22 |
| 4 | some | placebo | 1 | 0 | 1 | 1 | 4 | 1 | 1 | 0 | 10 | 19 |
| 4 | some | a | 0 | 0 | 0 | 1 | 0 | 2 | 2 | 1 | 13 | 19 |
| 4 | some | b | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 | 11 | 20 |
| 4 | some | ba | 1 | 0 | 0 | 0 | 0 | 2 | 2 | 2 | 14 | 21 |

```
proc catmod;
   weight count;
   response 0 .125 .25 .375 .5 .625 .75 .875 1;
   model no_hours =  center initial treat
                     treat*initial;
run;
```

**Output 14.5** Preliminary ANOVA Table

| Source | DF | Chi-Square | Prob |
|---|---|---|---|
| INTERCEPT | 1 | 5271.98 | <.0001 |
| CENTER | 3 | 29.02 | <.0001 |
| INITIAL | 1 | 62.65 | <.0001 |
| TREAT | 3 | 92.15 | <.0001 |
| INITIAL*TREAT | 3 | 12.63 | 0.0055 |
| RESIDUAL | 21 | 26.90 | 0.1743 |

```
model no_hours =  center initial treat(initial);
```

**Outputs 14.6 and 14.7** Nested Value ANOVA Table and Parameter Estimates

ANALYSIS-OF-VARIANCE TABLE

| Source | DF | Chi-Square | Prob |
|---|---|---|---|
| INTERCEPT | 1 | 5271.98 | <.0001 |
| CENTER | 3 | 29.02 | <.0001 |
| INITIAL | 1 | 62.65 | <.0001 |
| TREAT(INITIAL) | 6 | 102.70 | <.0001 |
| RESIDUAL | 21 | 26.90 | 0.1743 |

ANALYSIS OF WEIGHTED-LEAST-SQUARES ESTIMATES

| Effect | Parameter | Estimate | Standard Error | Chi-Square | Prob |
|---|---|---|---|---|---|
| INTERCEPT | | 0.6991 | 0.00963 | 5271.98 | <.0001 |
| CENTER | 1 | -0.0484 | 0.0145 | 11.24 | 0.0008 |
| | 2 | 0.0187 | 0.0145 | 1.66 | 0.1982 |
| | 3 | -0.0415 | 0.0176 | 5.56 | 0.0184 |
| INITIAL | lot | -0.0753 | 0.00951 | 62.65 | <.0001 |
| TREAT(INITIAL) | placebo lot | -0.1739 | 0.0283 | 37.81 | <.0001 |
| | treat_a lot | -0.0644 | 0.0255 | 6.39 | 0.0115 |
| | treat_b lot | 0.0952 | 0.0206 | 21.45 | <.0001 |
| | placebo some | -0.1159 | 0.0284 | 16.68 | <.0001 |
| | treat_a some | 0.00740 | 0.0217 | 0.12 | 0.7331 |
| | treat_b some | 0.0347 | 0.0206 | 2.84 | 0.0921 |

Table 14.5 Parameter Interpretations

| CATMOD Parameter | Model Parameter | Interpretation |
|---|---|---|
| 1 | $\alpha$ | intercept |
| 2 | $\beta_1$ | differential effect for center 1 |
| 3 | $\beta_2$ | differential effect for center 2 |
| 4 | $\beta_3$ | differential effect for center 3 |
| 5 | $\beta_4$ | differential effect for a lot of initial pain |
| 6 | $\beta_5$ | differential effect for placebo for a lot of pain |
| 7 | $\beta_6$ | differential effect for treatment a for a lot of pain |
| 8 | $\beta_7$ | differential effect for treatment b for a lot of pain |
| 9 | $\beta_8$ | differential effect for placebo for some pain |
| 10 | $\beta_9$ | differential effect for treatment a for some pain |
| 11 | $\beta_{10}$ | differential effect for treatment b for some pain |

Table 14.6 Hypothesis Tests

| Hypothesis | Initial Pain | Contrast | Coefficients $\beta_5$ | $\beta_6$ | $\beta_7$ | $\beta_8$ | $\beta_9$ | $\beta_{10}$ |
|---|---|---|---|---|---|---|---|---|
| treatment a vs. placebo | a lot | $-\beta_5+\beta_6$ | −1 | 1 | 0 | 0 | 0 | 0 |
| treatment b vs. placebo | a lot | $-\beta_5+\beta_7$ | −1 | 0 | 1 | 0 | 0 | 0 |
| treatment ba vs. placebo | a lot | $-2\beta_5-\beta_6-\beta_7$ | −2 | −1 | −1 | 0 | 0 | 0 |
| treatment ba vs. a | a lot | $-\beta_5-2\beta_6-\beta_7$ | −1 | −2 | −1 | 0 | 0 | 0 |
| treatment ba vs. b | a lot | $-\beta_5-\beta_6-2\beta_7$ | −1 | −1 | −2 | 0 | 0 | 0 |
| treatment a vs. placebo | some | $-\beta_8+\beta_9$ | 0 | 0 | 0 | −1 | 1 | 0 |
| treatment b vs. placebo | some | $-\beta_8+\beta_{10}$ | 0 | 0 | 0 | −1 | 0 | 1 |
| treatment ba vs. placebo | some | $-2\beta_8-\beta_9-\beta_{10}$ | 0 | 0 | 0 | −2 | −1 | −1 |
| treatment ba vs. a | some | $-\beta_8-2\beta_9-\beta_{10}$ | 0 | 0 | 0 | −1 | −2 | −1 |
| treatment ba vs. b | some | $-\beta_8-\beta_9-2\beta_{10}$ | 0 | 0 | 0 | −1 | −1 | −2 |

```
contrast 'lot: a-placebo'  treat(initial) -1  1  0  0  0  0 ;
contrast 'lot: b-placebo'  treat(initial) -1  0  1  0  0  0 ;
contrast 'lot: ba-placebo' treat(initial) -2 -1 -1  0  0  0 ;
contrast 'lot: ba-a'       treat(initial) -1 -2 -1  0  0  0 ;
contrast 'lot: ba-b'       treat(initial) -1 -1 -2  0  0  0 ;
contrast 'some:a-placebo'  treat(initial)  0  0  0 -1  1  0 ;
contrast 'some:b-placebo'  treat(initial)  0  0  0 -1  0  1 ;
contrast 'some:ba-placebo' treat(initial)  0  0  0 -2 -1 -1 ;
contrast 'some:ba-a'       treat(initial)  0  0  0 -1 -2 -1 ;
contrast 'some:ba-b'       treat(initial)  0  0  0 -1 -1 -2 ;
```

## **Output 14.8** Contrast Results

Analysis of Contrasts

| Contrast | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| lot: a-placebo | 1 | 5.59 | 0.0180 |
| lot: b-placebo | 1 | 42.81 | <.0001 |
| lot: ba-placebo | 1 | 61.48 | <.0001 |
| lot: ba-a | 1 | 32.06 | <.0001 |
| lot: ba-b | 1 | 2.59 | 0.1076 |
| some:a-placebo | 1 | 8.19 | 0.0042 |
| some:b-placebo | 1 | 12.83 | 0.0003 |
| some:ba-placebo | 1 | 21.45 | <.0001 |
| some:ba-a | 1 | 4.37 | 0.0365 |
| some:ba-b | 1 | 1.67 | 0.1964 |

Table 14.7 Hypothesis Tests

| **Hypothesis** | **Coefficients** | | | | | |
|---|---|---|---|---|---|---|
| | $\beta_5$ | $\beta_6$ | $\beta_7$ | $\beta_8$ | $\beta_9$ | $\beta_{10}$ |
| treatment a vs. placebo, some vs. a lot | – 1 | 1 | 0 | 1 | – 1 | 0 |
| treatment b vs. placebo, some vs. a lot | – 1 | 0 | 1 | 1 | 0 | – 1 |
| treatment ba vs. placebo, some vs. a lot | – 2 | – 1 | – 1 | 2 | 1 | 1 |
| treatment ba vs. a, some vs. a lot | – 1 | – 2 | – 1 | 1 | 2 | 1 |
| treatment ba vs. b, some vs. a lot | – 1 | – 1 | – 2 | 1 | 1 | 2 |
| average treatment a effect | – 1 | 1 | 0 | – 1 | 1 | 0 |
| average treatment b effect | – 1 | 0 | 1 | – 1 | 0 | 1 |
| average treatment ba effect | – 2 | – 1 | – 1 | – 2 | – 1 | – 1 |
| average ba vs. a | – 1 | – 2 | – 1 | – 1 | – 2 | – 1 |
| average ba vs. b | – 1 | – 1 | – 2 | – 1 | – 1 | – 2 |

The next block of CONTRAST statements performs these tests. The last two CONTRAST statements request the 3 df TREAT*INITIAL interaction and the 3 df TREAT effect, respectively. The output is displayed in Output 14.9.

```
contrast 'interact:a-placebo'     treat(initial) -1  1  0  1 -1  0 ;
contrast 'interact:b-placebo'     treat(initial) -1  0  1  1  0 -1 ;
contrast 'interact:ba-placebo'    treat(initial) -2 -1 -1  2  1  1 ;
contrast 'interact:ba-a'          treat(initial)   -1 -2 -1  1  2  1 ;
contrast 'interact:ba-b'          treat(initial)   -1 -1 -2  1  1  2 ;
contrast 'average:a-placebo'      treat(initial) -1  1  0 -1  1  0 ;
contrast 'average:b-placebo'      treat(initial) -1  0  1 -1  0  1 ;
contrast 'average:ba-placebo'     treat(initial) -2 -1 -1 -2 -1 -1 ;
contrast 'average:ba-a'           treat(initial) -1 -2 -1 -1 -2 -1 ;
contrast 'average:ba-b'           treat(initial) -1 -1 -2 -1 -1 -2 ;
contrast 'interaction'            treat(initial) -1  1  0  1 -1  0 ,
                                  treat(initial) -1  0  1  1  0 -1 ,
                                treat(initial) -2 -1 -1  2  1  1 ;
contrast 'treatment effect'       treat(initial) -1  1  0 -1  1  0 ,
                                  treat(initial) -1  0  1 -1  0  1 ,
                                treat(initial) -2 -1 -1 -2 -1 -1 ;
```

## **Output 14.9** Contrast Results

Analysis of Contrasts

| Contrast | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| interact:a-placebo | 1 | 0.05 | 0.8266 |
| interact:b-placebo | 1 | 4.05 | 0.0441 |
| interact:ba-placebo | 1 | 4.89 | 0.0271 |
| interact:ba-a | 1 | 8.61 | 0.0033 |
| interact:ba-b | 1 | 0.04 | 0.8344 |
| average:a-placebo | 1 | 13.51 | 0.0002 |
| average:b-placebo | 1 | 50.93 | <.0001 |
| average:ba-placebo | 1 | 77.60 | <.0001 |
| average:ba-a | 1 | 31.42 | <.0001 |
| average:ba-b | 1 | 4.22 | 0.0399 |
| interaction | 3 | 12.63 | 0.0055 |
| treatment effect | 3 | 92.15 | <.0001 |

## 14.7 Repeated Measurements Analysis

- Many studies have research designs that involve multiple measurements of a response over time.

- This section describes methods for analyzing repeated measurements data with weighted least squares

The following data are from Grizzle, Starmer, Koch (1969)

| | F = Favorable, U = Unfavorable | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Drug A response | F | F | F | F | U | U | U | U | |
| Drug B response | F | F | U | U | F | F | U | U | |
| Drug C response | F | U | F | U | F | U | F | U | Total |
| Number of subjects | 6 | 16 | 2 | 4 | 2 | 4 | 6 | 6 | 46 |

The hypothesis that the marginal distribution of the response variable is the same for all of the repeated measurement factor is called *marginal homogeneity*.

For one population, when you are analyzing marginal probabilities, the test of marginal homogeneity is the test of the main effect of the repeated measurement factor.

# WLS Methods for Repeated Measurements

- single subpopulation
- $r = 2^3 = 8$ response profiles
- three correlated marginal proportions of interest are *Pr*{favorable for Drug A}, *Pr*{favorable for Drug B}, and *Pr*{favorable for Drug C}
- Analyzing these functions answers the question of whether there is a difference between the three drugs (conditions).

# WLS Methods for Repeated Measurements

If $p$ represents the proportion vector corresponding to the row of counts, then you can compute the desired marginal proportions with a linear transformation

$$\boldsymbol{F}(\boldsymbol{p}) = \boldsymbol{A}\boldsymbol{p} = \begin{bmatrix} \boldsymbol{F}_1(\boldsymbol{p}) \\ \boldsymbol{F}_2(\boldsymbol{p}) \\ \boldsymbol{F}_3(\boldsymbol{p}) \end{bmatrix} =$$

$$\boldsymbol{A}\boldsymbol{p} = \begin{bmatrix} 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 \end{bmatrix} \begin{bmatrix} P_{FFF} \\ P_{FFU} \\ P_{FUF} \\ P_{FUU} \\ P_{UFF} \\ P_{UFU} \\ P_{UUF} \\ P_{UUU} \end{bmatrix}$$

The hypothesis of marginal homogeneity can now be addressed by fitting models of the form $\boldsymbol{F}(\boldsymbol{\pi}) = \boldsymbol{X}\boldsymbol{\beta}$, where $\boldsymbol{X}$ is a known model matrix and $\boldsymbol{\beta}$ is a vector of unknown parameters.

# Using PROC CATMOD for Repeated Measurements Analysis

- Specify the repeated measures as a crossed effect on the left-hand side of the MODEL statement.

- The rightmost variable on the left hand side of the MODEL statement varies fastest and the leftmost variable varies slowest.

- The keyword _RESPONSE_ specifies that the variation among the dependent variables is to be modeled.

# Using PROC CATMOD for Repeated Measurements Analysis

- The REPEATED statement specifies a name for each repeated measurement factor and can also be used to specify the type (numeric or character), number of levels, and the identification of each level.

- The ONEWAY option prints one-way marginal frequency distributions for each response variable in the MODEL statement.

## 14.7.2 One Population, Dichotomous Response

The following statements create SAS data set DRUG.

```
data drug;
     input druga $ drugb $ drugc $ count;
     datalines;
F  F  F  6
F  F  U 16
F  U  F  2
F  U  U  4
U  F  F  2
U  F  U  4
U  U  F  6
U  U  U  6
;
```

These statements request a repeated measurements analysis.

```
proc catmod;
        weight count;
        response marginals;
        model druga*drugb*drugc=_response_ / oneway cov;
        repeated drug 3 / _response_=drug;
run;
```

One-Way Frequencies

| Variable | Value | Frequency |
|---|---|---|
| druga | F | 28 |
| | U | 18 |
| drugb | F | 28 |
| | U | 18 |
| drugc | F | 16 |
| | U | 30 |

| Sample | Sample Size |
|---|---|
| 1 | 46 |

Response Profiles

| Response | druga | drugb | drugc |
|---|---|---|---|
| 1 | F | F | F |
| 2 | F | F | U |
| 3 | F | U | F |
| 4 | F | U | U |
| 5 | U | F | F |
| 6 | U | F | U |
| 7 | U | U | F |
| 8 | U | U | U |

| Sample | Function Number | Response Function | Design Matrix 1 | 2 | 3 |
|---|---|---|---|---|---|
| 1 | 1 | 0.60870 | 1 | 1 | 0 |
| | 2 | 0.60870 | 1 | 0 | 1 |
| | 3 | 0.34783 | 1 | -1 | -1 |

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 146.84 | <.0001 |
| drug | 2 | 6.58 | 0.0372 |
| Residual | 0 | . | . |

Analysis of Weighted Least Squares Estimates

| Effect | Parameter | Estimate | Standard Error | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|
| Intercept | 1 | 0.5217 | 0.0431 | 146.84 | <.0001 |
| drug | 2 | 0.0870 | 0.0507 | 2.95 | 0.0861 |
| | 3 | 0.0870 | 0.0507 | 2.95 | 0.0861 |

- Section 14.7.3 (Pages 471-478) provides an example of WLS analysis of repeated measures when there are more than two response levels and the repeated measurement factor is not time.

## 14.7.4 One Population Regression Analysis of Logits

- In longitudinal study of health effects of air pollution (Ware, Lipsitz, and Speizer 1988) children were examined annually at ages 9, 10, 11, 12

- At each examination, response measured was presence of wheezing. Interested in following questions:
  - Does prevalence of wheezing change with age?
  - Is there a quantifiable trend in age-specific prevalence rates?
- The following data are from 1019 children included in study. In this single population example, crossclassification of dichotomous outcome at 4 time points defines

$$r = 2^4 = 16 \text{ response profiles}$$

Table 14.8 Breath Test Results at Four Ages

| Wheeze | | | | No. of Children |
|---|---|---|---|---|
| Age 9 | Age 10 | Age 11 | Age 12 | |
| Present | Present | Present | Present | 94 |
| Present | Present | Present | Absent | 30 |
| Present | Present | Absent | Present | 15 |
| Present | Present | Absent | Absent | 28 |
| Present | Absent | Present | Present | 14 |
| Present | Absent | Present | Absent | 9 |
| Present | Absent | Absent | Present | 12 |
| Present | Absent | Absent | Absent | 63 |
| Absent | Present | Present | Present | 19 |
| Absent | Present | Present | Absent | 15 |
| Absent | Present | Absent | Present | 10 |
| Absent | Present | Absent | Absent | 44 |
| Absent | Absent | Present | Present | 17 |
| Absent | Absent | Present | Absent | 42 |
| Absent | Absent | Absent | Present | 35 |
| Absent | Absent | Absent | Absent | 572 |

```
proc catmod order=data;
  weight count;
  response marginals;
  model wheeze9*wheeze10*wheeze11*wheeze12=_response_
        / oneway;
  repeated age;
run;
```

**Output 14.10** One-Way Frequency Distributions

One-Way Frequencies

| Variable | Value | Frequency |
|---|---|---|
| wheeze9 | Present | 265 |
| | Absent | 754 |
| wheeze10 | Present | 255 |
| | Absent | 764 |
| wheeze11 | Present | 240 |
| | Absent | 779 |
| wheeze12 | Present | 216 |
| | Absent | 803 |

## **Output 14.11** Response Functions and Model Matrix

| Sample | Function Number | Response Function | Design Matrix 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|
| 1 | 1 | 0.26006 | 1 | 1 | 0 | 0 |
| | 2 | 0.25025 | 1 | 0 | 1 | 0 |
| | 3 | 0.23553 | 1 | 0 | 0 | 1 |
| | 4 | 0.21197 | 1 | -1 | -1 | -1 |

## **Output 14.12** Analysis-of-Variance Table

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 523.63 | <.0001 |
| age | 3 | 12.85 | 0.0050 |
| Residual | 0 | . | . |

Could have manually specified the Linear Model:

```
proc catmod order=data;
         weight count;
         response marginals;
         model wheeze9*wheeze10*wheeze11*wheeze12= (1  9,
                                                    1  10,
                                                    1  11,
                                                    1  12)
                                                (1=Intercept',
                                                 2='Linear Age')
                                                 / noprofile design;
run;
```

**Output 14.13** Response Functions and Model Matrix

| Sample | Function Number | Response Function | Design Matrix 1 | 2 |
|---|---|---|---|---|
| 1 | 1 | 0.26006 | 1 | 9 |
| | 2 | 0.25025 | 1 | 10 |
| | 3 | 0.23553 | 1 | 11 |
| | 4 | 0.21197 | 1 | 12 |

## **Output 14.14** ANOVA Table

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 66.70 | <.0001 |
| Linear Age | 1 | 12.31 | 0.0005 |
| Residual | 2 | 0.54 | 0.7620 |

## **Output 14.15** Parameter Estimates

Analysis of Weighted Least Squares Estimates

| Effect | Parameter | Estimate | Standard Error | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|
| Model | 1 | 0.4083 | 0.0500 | 66.70 | <.0001 |
| | 2 | -0.0161 | 0.00460 | 12.31 | 0.0005 |

Specify a logit transformation of the probabilities:

```
proc catmod order=data;
         weight count;
         response logits;
         model wheeze9*wheeze10*wheeze11*wheeze12= (1  9,
                                                    1  10,
                                                    1  11,
                                                    1  12)
                                                (1=Intercept',
                                                 2='Linear Age')
                                                 / noprofile design;
run;
```

**Output 14.16** Response Functions and Model Matrix

| Sample | Function Number | Response Function | Design Matrix 1 | 2 |
|---|---|---|---|---|
| 1 | 1 | -1.04566 | 1 | 9 |
| | 2 | -1.09730 | 1 | 10 |
| | 3 | -1.17737 | 1 | 11 |
| | 4 | -1.31308 | 1 | 12 |

## **Output 14.17** ANOVA Table

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 0.76 | 0.3824 |
| Linear Age | 1 | 11.77 | 0.0006 |
| Residual | 2 | 0.67 | 0.7167 |

## **Output 14.18** Parameter Estimates

Analysis of Weighted Least Squares Estimates

| Effect | Parameter | Estimate | Standard Error | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|
| Model | 1 | -0.2367 | 0.2710 | 0.76 | 0.3824 |
| | 2 | -0.0879 | 0.0256 | 11.77 | 0.0006 |

Example: Study to compare test treatment and placebo for management of a respiratory disorder (Reference: Koch, Carr, Amara, Stokes, and Uryniak [1990])

1. Two centers
2. Four visits
3. Ordered global response with 5 categories (terrible, poor, fair, good, excellent as scores 0,1,2,3,4)
4. Age, gender, baseline are covariables

Partial Listing of Data from a Multicenter, Multivisit Clinical Trial to Compare Two Treatments for Patients with a Respiratory Disorder (Reference: Koch *et al* [1990])

| Center | Patient | Drug | Sex | Age | Base | Visit 1 | Visit 2 | Visit 3 | Visit 4 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 53 | A | F | 32 | 1 | 2 | 2 | 4 | 2 |
| | 18 | A | F | 47 | 2 | 2 | 3 | 4 | 4 |
| | 54 | A | M | 11 | 4 | 4 | 4 | 4 | 2 |
| | 12 | A | M | 14 | 2 | 3 | 3 | 3 | 2 |
| | 51 | A | M | 15 | 0 | 2 | 3 | 3 | 3 |
| | 20 | A | M | 20 | 3 | 3 | 2 | 3 | 1 |
| | 16 | A | M | 22 | 1 | 2 | 2 | 2 | 3 |
| | 50 | A | M | 22 | 2 | 1 | 3 | 4 | 4 |
| | 03 | A | M | 23 | 3 | 3 | 4 | 4 | 3 |
| | 32 | A | M | 23 | 2 | 3 | 4 | 4 | 4 |
| | 56 | A | M | 25 | 2 | 3 | 3 | 2 | 3 |
| | 35 | A | M | 26 | 1 | 2 | 2 | 3 | 2 |
| | 26 | A | M | 26 | 2 | 2 | 2 | 2 | 2 |
| | 21 | A | M | 26 | 2 | 4 | 1 | 4 | 2 |
| | 08 | A | M | 28 | 1 | 2 | 2 | 1 | 2 |
| | 30 | A | M | 28 | 0 | 0 | 1 | 2 | 1 |
| | 33 | A | M | 30 | 3 | 3 | 4 | 4 | 2 |
| | 11 | A | M | 30 | 3 | 4 | 4 | 4 | 3 |

# WLS FOR CATEGORICAL DATA: EXAMPLE USING CHAPTER 13 DATA WITH BINARY RESPONSE MEASURED AT FOUR VISITS

```
/* Model with Interactions */
PROC CATMOD;
  RESPONSE LOGITS;
  POPULATION CENTER DRUG;
  MODEL VIS1_BIN*VIS2_BIN*VIS3_BIN*VIS4_BIN =
              CENTER|DRUG CENTER|_RESPONSE_
              DRUG|_RESPONSE_
                / NODESIGN NOPARM NOPROFILE;
  REPEATED TIME;
RUN;
```

CATMOD PROCEDURE

| | | | |
|---|---|---|---|
| Response | vis1_*vis2_*vis3_*vis4_b | Response Levels | 15 |
| Weight Variable | None | Populations | 4 |
| Data Set | CH13T | Total Frequency | 111 |
| Frequency Missing | 0 | Observations | 111 |

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 3.34 | 0.0678 |
| center | 1 | 8.37 | 0.0038 |
| drug | 1 | 10.92 | 0.0010 |
| center*drug | 1 | 1.18 | 0.2770 |
| time | 3 | 3.86 | 0.2769 |
| center*time | 3 | 3.82 | 0.2821 |
| drug*time | 3 | 2.74 | 0.4338 |
| Residual | 3 | 0.59 | 0.8994 |

```
/* MAIN EFFECTS MODEL */
PROC CATMOD;
  RESPONSE LOGITS;
  POPULATION CENTER DRUG;
  MODEL VIS1_BIN*VIS2_BIN*VIS3_BIN*VIS4_BIN =CENTER
          DRUG _RESPONSE_ / NODESIGN NOPROFILE;
  REPEATED TIME;
RUN;
```

The CATMOD Procedure

| | | | |
|---|---|---|---|
| Response | vis1_*vis2_*vis3_*vis4_b | Response Levels | 15 |
| Weight Variable | None | Populations | 4 |
| Data Set | CH13T | Total Frequency | 111 |
| Frequency Missing | 0 | Observations | 111 |

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 1.68 | 0.1947 |
| center | 1 | 7.62 | 0.0058 |
| drug | 1 | 10.61 | 0.0011 |
| time | 3 | 2.76 | 0.4303 |
| Residual | 10 | 13.04 | 0.2212 |

Analysis of Weighted Least Squares Estimates

| Effect | Parameter | Estimate | Standard Error | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|
| Intercept | 1 | -0.2041 | 0.1574 | 1.68 | 0.1947 |
| center | 2 | 0.4401 | 0.1594 | 7.62 | 0.0058 |
| drug | 3 | 0.5217 | 0.1602 | 10.61 | 0.0011 |
| time | 4 | -0.1159 | 0.1261 | 0.85 | 0.3579 |
| | 5 | 0.0856 | 0.1147 | 0.56 | 0.4554 |
| | 6 | -0.0754 | 0.1129 | 0.45 | 0.5038 |

# RESPIRATORY DISORDER DATA

Model with Default Coding for Mean Score Response with All Interactions

```
PROC CATMOD;
  RESPONSE MEAN;
  MODEL VISIT1*VISIT2*VISIT3*VISIT4 = DRUG|CENTER|_RESPONSE_/COV;
  REPEATED TIME;
RUN;
```

The CATMOD Procedure
Data Summary

| | | | |
|---|---|---|---|
| Response | visit*visit*visit*visit4 | Response Levels | 67 |
| Weight Variable | None | Populations | 4 |
| Data Set | CH13T2 | Total Frequency | 111 |
| Frequency Missing | 0 | Observations | 111 |

Response Functions and Covariance Matrix

| Sample | Function Number | Response Function | Covariance Matrix 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|
| 1 | 1 | 2.24138 | 0.06101 | 0.04875 | 0.05031 | 0.04371 |
| | 2 | 2.00000 | 0.04875 | 0.05945 | 0.04400 | 0.03686 |
| | 3 | 2.24138 | 0.05031 | 0.04400 | 0.06815 | 0.05560 |
| | 4 | 2.03448 | 0.04371 | 0.03686 | 0.05560 | 0.05584 |
| 2 | 1 | 2.82143 | 0.03330 | 0.01713 | 0.01667 | 0.01827 |
| | 2 | 2.28571 | 0.01713 | 0.0583 | 0.05266 | 0.05649 |
| | 3 | 2.21429 | 0.01667 | 0.05266 | 0.07744 | 0.07425 |
| | 4 | 2.46429 | 0.01827 | 0.05649 | 0.07425 | 0.09052 |
| 3 | 1 | 2.51852 | 0.03394 | 0.01793 | 0.01590 | 0.00996 |
| | 2 | 2.85185 | 0.01793 | 0.03485 | 0.01956 | 0.02185 |
| | 3 | 2.81481 | 0.01590 | 0.01956 | 0.04948 | 0.02251 |
| | 4 | 2.48148 | 0.00996 | 0.02185 | 0.02251 | 0.03942 |
| 4 | 1 | 3.33333 | 0.02469 | 0.01829 | 0.01555 | 0.02012 |
| | 2 | 3.40741 | 0.01829 | 0.03363 | 0.02845 | 0.02764 |
| | 3 | 3.29630 | 0.01555 | 0.02845 | 0.03516 | 0.02733 |
| | 4 | 3.25926 | 0.02012 | 0.02764 | 0.02733 | 0.05375 |

# ANOVA Table

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 767.19 | <.0001 |
| drug | 1 | 13.76 | 0.0002 |
| center | 1 | 6.53 | 0.0106 |
| drug*center | 1 | 0.80 | 0.3724 |
| time | 3 | 2.40 | 0.4929 |
| drug*time | 3 | 12.60 | 0.0056 |
| center*time | 3 | 8.13 | 0.0433 |
| drug*center*time | 3 | 0.58 | 0.9010 |
| Residual | 0 | . | . |

Many studies have response variables with ordinal data for which only rankings are meaningful.

1. Ordered categorical response variables
   a. Arbitrary scores may not be meaningful
   b. Models such as the proportional odds model may have unsatisfactory goodness of fit
2. Response variables with continuous scales can have skewed distributions and/or outliers to an extent that contradicts a metric scale and thereby differences and/or other functions of observed values may not be meaningful. In these situations, analyses involving rank measures of association are potentially of interest.

Combined use of FREQ and CATMOD for analysis of Mann-Whitney estimators from a study with eight strata for the comparison of two treatments for an ordered categorical response variable (Reference: Stokes *et al* [2000]).

| Diagnostic Class | Investigator | Treatment | Patient Status | | | | |
|---|---|---|---|---|---|---|---|
| | | | Poor | Fair | Moderate | Good | Excellent |
| I | A | Placebo | 7 | 0 | 1 | 1 | 1 |
| I | A | Active | 3 | 2 | 2 | 1 | 0 |
| I | B | Placebo | 5 | 4 | 2 | 3 | 3 |
| I | B | Active | 1 | 6 | 1 | 5 | 3 |
| II | A | Placebo | 1 | 1 | 0 | 1 | 1 |
| II | A | Active | 1 | 0 | 1 | 2 | 2 |
| II | B | Placebo | 3 | 1 | 1 | 5 | 0 |
| II | B | Active | 0 | 1 | 1 | 1 | 6 |
| III | A | Placebo | 5 | 0 | 0 | 8 | 1 |
| III | A | Active | 2 | 0 | 3 | 3 | 2 |
| III | B | Placebo | 2 | 5 | 1 | 4 | 2 |
| III | B | Active | 2 | 4 | 1 | 10 | 3 |
| IV | A | Placebo | 5 | 0 | 3 | 3 | 0 |
| IV | A | Active | 8 | 1 | 3 | 4 | 0 |
| IV | B | Placebo | 3 | 4 | 3 | 4 | 2 |
| IV | B | Active | 1 | 5 | 2 | 3 | 1 |

FREQ is used to obtain Somer's D and corresponding standard error for each of the eight strata according to (Diagnostic Class $\times$ Investigators).

$U = \frac{(\text{Somer's } D \; C|R)+1}{2}$ and $S = \frac{SE(D)}{2}$ are used to obtain the Mann-Whitney estimators and their standard errors. The respective estimates for the eight strata are independent.

| Diagnostic Class | Researcher | Somer's $D$ | ASE | $U_i$ | $S_i$ |
|---|---|---|---|---|---|
| I | A | 0.2000 | 0.3515 | 0.6000 | 0.1758 |
| I | B | 0.2002 | 0.1915 | 0.6001 | 0.0958 |
| II | A | 0.2083 | 0.3622 | 0.6042 | 0.1811 |
| II | B | 0.6778 | 0.1834 | 0.8389 | 0.0917 |
| III | A | 0.0260 | 0.2271 | 0.5130 | 0.1136 |
| III | B | 0.1893 | 0.1923 | 0.5947 | 0.0962 |
| IV | A | 0.0000 | 0.2007 | 0.5000 | 0.1004 |
| IV | B | -0.0156 | 0.2116 | 0.4922 | 0.1058 |

The variation among the Mann-Whitney estimators is analyzed by weighted least squares methods through CATMOD.

The input for this analysis and the specification of a model that addresses the effects of diagnosis and investigator on the association between treatment and response are as follows:

```
data MannWhitney;
       input b1-b8 _type_ $ _name_ $8.;
       datalines;
    .6000  .6011  .6042 .8389 .5130 .5947 .5000 .4922 parms
    .03091 .0000  .0000 .0000 .0000 .0000 .0000 .0000 cov b1
    .0000  .00918 .0000 .0000 .0000 .0000 .0000 .0000 cov b2
    .0000  .0000  .3280 .0000 .0000 .0000 .0000 .0000 cov b3
    .0000  .0000  .0000 .0084 .0000 .0000 .0000 .0000 cov b4
    .0000  .0000  .0000 .0000 .0129 .0000 .0000 .0000 cov b5
    .0000  .0000  .0000 .0000 .0000 .0093 .0000 .0000 cov b6
    .0000  .0000  .0000 .0000 .0000 .0000 .0101 .0000 cov b7
    .0000  .0000  .0000 .0000 .0000 .0000 .0000 .0112 cov b8
    ;
```

```
proc catmod data=MannWhitney;
          response read b1-b8;
          factors diagnosis $ 4 , invest $ 2 /
             _response_ = diagnosis invest
          profile = (I   A,
                     I   B,
                     II  A,
                     II  B,
                     III A,
                     III B,
                     IV  A,
                     IV  B);
          model _f_ = _response_ / cov;
     run;
```

The resulting test statistics from this analysis are as follows:

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Intercept | 1 | 193.69 | <.0001 |
| diagnosis | 3 | 6.98 | 0.0725 |
| invest | 1 | 0.14 | 0.7122 |
| Residual | 3 | 0.33 | 0.9540 |

Since there is essentially no variation among the Mann-Whitney estimators across the eight strata, a model which specifies a homogenous value is applied.

```
model _f_ = ( 1 ,
              1 ,
              1 ,
              1 ,
              1 ,
              1 ,
              1 ,
              1 ) ;
```

The results for this model for homogenous association between treatment and response are as follows:

Analysis of Variance

| Source | DF | Chi-Square | Pr > ChiSq |
|---|---|---|---|
| Model\|Mean | 0 | . | . |
| Residual | 7 | 9.41 | 0.2247 |

Analysis of Weighted Least Squares Estimates

| Effect | Parameter | Estimate | Standard Error | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|
| Model | 1 | 0.6027 | 0.0396 | 231.30 | <.0001 |

The resulting Mann-Whitney estimator of 0.60 is interpretable as the probability of better response for a randomly selected patient with active treatment than placebo. Note that the test statistic for this association is about

$$Z = \{(0.6027 - 0.5) / 0.0396\} = 2.59$$

And has two-sided p-value 0.0095.

Van Elteren test from PROC FREQ:

$$Q = 3.89, p = 0.0486$$