

# Supplement to Session 6

## **S6.2 Grouped data**

### **S6.2.1 Observed and expected frequencies**

```
* Set up formats for GCS at entry and outcome *;  
  
proc format;  
  value gcsfmt 1 = 'GCS 3-5'  
            2 = 'GCS 6-8';  
  value gosfmt 1 = 'Good'  
            2 = 'Mod Dis'  
            3 = 'Severe Dis'  
            4 = 'Vegetative'  
            5 = 'Dead';  
run;  
  
* Read in grouped data from severe head injury study (example 1) *;  
  
data head1;  
format gcsentry gcsfmt. gos gosfmt.;  
input gcsentry gos frequency;  
cards;  
1 1 73  
1 2 55  
1 3 79  
1 4 37  
1 5 358  
2 1 219  
2 2 118  
2 3 66  
2 4 10  
2 5 92  
;  
run;  
  
* Fit proportional odds model for more favourable outcome with *  
* GCS at entry and create dataset with original data, linear      *  
* predictors and standard errors, and predicted cumulative      *  
* probabilities                                         *;  
  
proc logistic data=head1;  
  weight frequency;  
  class gcsentry (ref='GCS 3-5') / param=ref order=internal;  
  model gos (order=internal) = gcsentry;  
  output out=fittedcum xbeta=xbeta stdxbeta=stdxbeta  
                    predprobs=cumulative;  
run;
```

Analysis of Maximum Likelihood Estimates

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept Good	$\hat{\alpha}_1$	1	<b>-2.1223</b>	0.1044	413.6292	<.0001
Intercept Mod Dis	$\hat{\alpha}_2$	1	<b>-1.2698</b>	0.0907	196.0272	<.0001
Intercept Severe Dis	$\hat{\alpha}_3$	1	<b>-0.6006</b>	0.0830	52.3620	<.0001
Intercept Vegetative	$\hat{\alpha}_4$	1	<b>-0.3861</b>	0.0816	22.3715	<.0001
gcsetry GCS 6-8	$\hat{\beta}$	1	<b>1.8984</b>	0.1210	246.1540	<.0001

GCS 3-5:  $\hat{\eta}(0) = 0$     GCS 6-8:  $\hat{\eta}(1) = 1.8984$

**xbeta=xbeta stdxbeta=stdxbeta (Linear Predictors)**

$$\alpha_k + \hat{\eta}(0)$$

Obs	gcsetry	gos	frequency	_LEVEL_	xbeta	stdxbeta
1	<b>GCS 3-5</b>	Good	73	Good	<b>-2.12226</b>	0.10435
2	<b>GCS 3-5</b>	Good	73	Mod Dis	<b>-1.26981</b>	0.09069
3	<b>GCS 3-5</b>	Good	73	Severe Dis	<b>-0.60063</b>	0.08300
4	<b>GCS 3-5</b>	Good	73	Vegetative	<b>-0.38610</b>	0.08163
5	GCS 3-5	Mod Dis	55	Good	-2.12226	0.10435
6	GCS 3-5	Mod Dis	55	Mod Dis	-1.26981	0.09069
7	GCS 3-5	Mod Dis	55	Severe Dis	-0.60063	0.08300
8	GCS 3-5	Mod Dis	55	Vegetative	-0.38610	0.08163
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
33	GCS 6-8	Vegetative	10	Good	-0.22381	0.08652
34	GCS 6-8	Vegetative	10	Mod Dis	0.62864	0.08882
35	GCS 6-8	Vegetative	10	Severe Dis	1.29782	0.09621
36	GCS 6-8	Vegetative	10	Vegetative	1.51235	0.09900
37	<b>GCS 6-8</b>	Dead	92	Good	<b>-0.22381</b>	0.08652
38	<b>GCS 6-8</b>	Dead	92	Mod Dis	<b>0.62864</b>	0.08882
39	<b>GCS 6-8</b>	Dead	92	Severe Dis	<b>1.29782</b>	0.09621
40	<b>GCS 6-8</b>	Dead	92	Vegetative	<b>1.51235</b>	0.09900

$$\alpha_k + \hat{\eta}(1)$$

**predprobs=cumulative (Predicted Cumulative Probabilities)**

$$\hat{Q}_1(0) = (1 + e^{-(2.1222)})^{-1}$$

$$\hat{Q}_2(0) = (1 + e^{-(1.2698)})^{-1}$$

Obs	gcsentry	frequency	CP_Good	CP_Mod_Dis	CP_Severe_Dis	CP_Vegetative	CP_Dead
1	GCS 3-5	73	0.10695	0.21929	0.35420	0.40466	1
2	GCS 3-5	73	0.10695	0.21929	0.35420	0.40466	1
3	GCS 3-5	73	0.10695	0.21929	0.35420	0.40466	1
4	GCS 3-5	73	0.10695	0.21929	0.35420	0.40466	1
5	GCS 3-5	55	0.10695	0.21929	0.35420	0.40466	1
6	GCS 3-5	55	0.10695	0.21929	0.35420	0.40466	1
7	GCS 3-5	55	0.10695	0.21929	0.35420	0.40466	1
8	GCS 3-5	55	0.10695	0.21929	0.35420	0.40466	1
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
33	GCS 6-8	10	0.44428	0.65218	0.78547	0.81941	1
34	GCS 6-8	10	0.44428	0.65218	0.78547	0.81941	1
35	GCS 6-8	10	0.44428	0.65218	0.78547	0.81941	1
36	GCS 6-8	10	0.44428	0.65218	0.78547	0.81941	1
37	GCS 6-8	92	0.44428	0.65218	0.78547	0.81941	1
38	GCS 6-8	92	0.44428	0.65218	0.78547	0.81941	1
39	GCS 6-8	92	0.44428	0.65218	0.78547	0.81941	1
40	<b>GCS 6-8</b>	92	<b>0.44428</b>	<b>0.65218</b>	<b>0.78547</b>	<b>0.81941</b>	<b>1</b>

$$\hat{Q}_3(1) = (1 + e^{-(1.2978)})^{-1}$$

$$\hat{Q}_4(1) = (1 + e^{-(1.5124)})^{-1}$$

$$\hat{Q}_5(1)$$

```

* Fit proportional odds model for more favourable outcome with *
* GCS at entry and create dataset with original data, linear      *
* predictors and standard errors, and predicted probabilities   *;
*;

proc logistic data=head1;
  weight frequency;
  class gcsentry (ref='GCS 3-5') / param=ref order=internal;
  model gos (order=internal) = gcsentry;
  output out=fittedind xbeta=xbeta stdxbeta=stdxbeta
           predprobs=individual;
run;

```

## **predprobs=individual (Predicted Probabilities)**

$$\hat{p}_1(0) = \hat{Q}_1(0)$$

$$\hat{p}_2(0) = \hat{Q}_2(0) - \hat{Q}_1(0)$$

Obs	gcsentry	frequency	IP_Good	IP_Mod_Dis	IP_Severe_Dis	IP_Vegetative	IP_Dead
1	GCS 3-5	73	0.10695	0.11234	0.13491	0.050457	0.59534
2	GCS 3-5	73	0.10695	0.11234	0.13491	0.050457	0.59534
3	GCS 3-5	73	0.10695	0.11234	0.13491	0.050457	0.59534
4	GCS 3-5	73	0.10695	0.11234	0.13491	0.050457	0.59534
5	GCS 3-5	55	0.10695	0.11234	0.13491	0.050457	0.59534
6	GCS 3-5	55	0.10695	0.11234	0.13491	0.050457	0.59534
7	GCS 3-5	55	0.10695	0.11234	0.13491	0.050457	0.59534
8	GCS 3-5	55	0.10695	0.11234	0.13491	0.050457	0.59534
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
33	GCS 6-8	10	0.44428	0.20790	0.13329	0.033942	0.18059
34	GCS 6-8	10	0.44428	0.20790	0.13329	0.033942	0.18059
35	GCS 6-8	10	0.44428	0.20790	0.13329	0.033942	0.18059
36	GCS 6-8	10	0.44428	0.20790	0.13329	0.033942	0.18059
37	GCS 6-8	92	0.44428	0.20790	0.13329	0.033942	0.18059
38	GCS 6-8	92	0.44428	0.20790	0.13329	0.033942	0.18059
39	GCS 6-8	92	0.44428	0.20790	0.13329	0.033942	0.18059
40	<b>GCS 6-8</b>	92	<b>0.44428</b>	<b>0.20790</b>	<b>0.13329</b>	<b>0.033942</b>	<b>0.18059</b>

$$\hat{p}_3(1) = \hat{Q}_3(1) - \hat{Q}_2(1)$$

$$\hat{p}_4(1) = \hat{Q}_4(1) - \hat{Q}_3(1)$$

$$\hat{p}_5(1) = 1 - \hat{Q}_4(1)$$

## Calculation of expected values

```
data obsexp;
set fitted1;

if _LEVEL_ = 1;

Obs_Good = frequency*(gos = 1);
Obs_Mod_Dis = frequency*(gos = 2);
Obs_Severe_Dis = frequency*(gos = 3);
Obs_Vegetative = frequency*(gos = 4);
Obs_Dead = frequency*(gos = 5);

Exp_Good = frequency*IP_Good;
Exp_Mod_Dis = frequency*IP_Mod_Dis;
Exp_Severe_Dis = frequency*IP_Severe_Dis;
Exp_Vegetative = frequency*IP_Vegetative;
Exp_Dead = frequency*IP_Dead;
run;

proc means data=obsexp sum;
var Obs_Good Exp_Good Obs_Mod_Dis Exp_Mod_Dis Obs_Severe_Dis
    Exp_Severe_Dis Obs_Vegetative Exp_Vegetative Obs_Dead Exp_Dead;
by gcseentry;
run;
```

----- gcseentry=GCS 3-5 -----

The MEANS Procedure

Variable	Sum
Obs_Good	73.0000000
Exp_Good	64.3851540
Obs_Mod_Dis	55.0000000
Exp_Mod_Dis	67.6271197
Obs_Severe_Dis	79.0000000
Exp_Severe_Dis	81.2162332
Obs_Vegetative	37.0000000
Exp_Vegetative	30.3753732
Obs_Dead	358.0000000
Exp_Dead	358.3961199

----- gcseentry=GCS 6-8 -----

Variable	Sum
Obs_Good	219.0000000
Exp_Good	224.3613533
Obs_Mod_Dis	118.0000000
Exp_Mod_Dis	104.9897991
Obs_Severe_Dis	66.0000000
Exp_Severe_Dis	67.3102907
Obs_Vegetative	10.0000000
Exp_Vegetative	17.1405085
Obs_Dead	92.0000000
Exp_Dead	91.1980484

## S6.2.2 Score test for proportional odds

Score Test for the Proportional Odds Assumption

Chi-Square	DF	Pr > ChiSq
<b>11.8845</b>	<b>3</b>	<b>0.0078</b>

Model Fit Statistics

Criterion	Intercept Only	Intercept and Covariates
AIC	3125.079	2860.319
SC	3126.289	2861.832
<b>-2 Log L</b>	<b>3117.079</b>	<b>2850.319</b>

Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept Good	1	<b>-2.1223</b>	0.1044	413.6292	<.0001
Intercept Mod Dis	1	<b>-1.2698</b>	0.0907	196.0272	<.0001
Intercept Severe Dis	1	<b>-0.6006</b>	0.0830	52.3620	<.0001
Intercept Vegetative	1	<b>-0.3861</b>	0.0816	22.3715	<.0001
gcsentry GCS 6-8	1	<b>1.8984</b>	0.1210	246.1540	<.0001

### **S6.3 Ungrouped data**

Data from head injury study (example 2) in head2 dataset. See supplement to session 2 for details of these data.

```
/* age (yrs) continuous
gcsmotor: 1 = None or extension
           2 = Abnormal or normal flexion
           3 = Localises
treat: 0 = Control
       1 = Treated
gos4: 1 = Good recovery
      2 = Moderate disability
      3 = Severe disability
      4 = Vegetative state or Dead
*/
* Fit proportional odds model for more favourable outcome with *
* age, GCS motor score and treatment and create dataset with   *
* original data, linear predictors and predicted probabilities *;

proc logistic data=head2;
  class gcsmotor (ref='1')
    treat (ref='0') / param=ref order=internal;
  model gos4 (order=internal) = age gcsmotor treat;
  output out=fitted2 xbeta=xbeta predprobs=individual;
run;

proc print data=fitted2 noobs;
  var patient age gcsmotor treat gos4 _LEVEL_ xbeta;
run;

* Calculate individual linear predictor for each patient using *
* estimate of alpha1 of -0.8217                                *;

data obsexp;
set fitted2;
if _LEVEL_ = 1;
eta = xbeta + 0.8217;
groupeta = (eta le -0.85) + (eta le -0.35) + (eta le 0.15) +
(eta le 0.65) + 1;
Obs1 = (gos4 = 1);
Obs2 = (gos4 = 2);
Obs3 = (gos4 = 3);
Obs4 = (gos4 = 4);

Exp1 = IP_1;
Exp2 = IP_2;
Exp3 = IP_3;
Exp4 = IP_4;
run;
```

```

proc print data=obsexp noobs;
  var patient age gcsmotor treat gos4 eta;
run;

proc sort data=obsexp;
  by groupeta;
run;

proc means data=obsexp sum nolabels;
  var Obs1 Exp1 Obs2 Exp2 Obs3 Exp3 Obs4 Exp4;
  by groupeta;
run;

```

Response Profile

Ordered Value	gos4	Total Frequency
1	1	113
2	2	57
3	3	60
4	4	111

Probabilities modeled are cumulated over the lower Ordered Values.

Class Level Information

Class	Value	Design Variables	
gcsmotor	1	0	0
	2	1	0
	3	0	1
treat	0	0	
	1	1	

Score Test for the Proportional Odds Assumption

Chi-Square	DF	Pr > ChiSq
5.4898	8	0.7042

Analysis of Maximum Likelihood Estimates

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept 1	$\hat{\alpha}_1$	1	<b>-0.8217</b>	0.2924	7.8956	0.0050
Intercept 2	$\hat{\alpha}_2$	1	<b>0.00116</b>	0.2878	0.0000	0.9968
Intercept 3	$\hat{\alpha}_3$	1	<b>0.8461</b>	0.2914	8.4323	0.0037
age	$\hat{\beta}_1$	1	<b>-0.0247</b>	0.00682	13.0823	0.0003
gcsmotor 2	$\hat{\beta}_2$	1	<b>0.5058</b>	0.2324	4.7387	0.0295
gcsmotor 3	$\hat{\beta}_3$	1	<b>1.9026</b>	0.2832	45.1285	<.0001
treat	$\hat{\beta}_4$	1	<b>0.6019</b>	0.2054	8.5885	0.0034

### S6.3.1 Observed and expected frequencies

From the model, each  $i^{\text{th}}$  patient has:

- an individual linear predictor:  $\eta(\underline{z}_i)$
- $m$  fitted probabilities:  $p_k(\underline{z}_i)$

SAS presents  $m - 1$  rows for each patient in the output data set:

**XBETA:**       $\alpha_k + \eta(\underline{z}_i)$        $k = 1, \dots, m - 1$

**IP\_1 – IP\_4:**  $\hat{p}_1(\underline{z}_i)$  to  $\hat{p}_4(\underline{z}_i)$

where

$$\hat{p}_k(\underline{z}_i) = \hat{Q}_k(\underline{z}_i) - \hat{Q}_{k-1}(\underline{z}_i)$$

$$\hat{Q}_k(\underline{z}_i) = (1 + e^{-(\hat{\alpha}_k + \hat{\eta}(\underline{z}_i))})^{-1}$$

## Linear Predictors

patient	age	gcsmotor	treat	gos4	_LEVEL_	xbeta
1	66	1	0	1	1	-2.44904
1	66	1	0	1	2	-1.62616
1	66	1	0	1	3	-0.78120
2	63	1	1	1	1	-1.77314
2	63	1	1	1	2	-0.95026
2	63	1	1	1	3	-0.10530
3	58	1	1	1	1	-1.64985
3	58	1	1	1	2	-0.82698
3	58	1	1	1	3	0.01798

etc.

from which  $\hat{\eta}(\underline{z}_i)$  can be calculated:

## Individual Linear Predictor

$$\hat{\eta}(\underline{z}_i) = \mathbf{X}\hat{\beta}\text{ETA} - \hat{\alpha}_1$$

Observed category

patient	age	gcsmotor	treat	gos4	eta
1	66	1	0	1	-1.62734
2	63	1	1	1	-0.95144
3	58	1	1	1	-0.82815
4	54	1	0	1	-1.33146
5	51	1	1	1	-0.65556
6	49	1	0	1	-1.20818
7	49	1	1	1	-0.60625
8	46	1	0	1	-1.13421
9	46	1	1	1	-0.53228
10	43	1	0	1	-1.06024

etc.

----- groupeta=1 -----

The MEANS Procedure

Variable	Sum
Obs1	46.000000
Expl	46.8542492
Obs2	13.000000
Exp2	11.7864356
Obs3	8.000000
Exp3	7.7482055
Obs4	7.000000
Exp4	7.6111096

----- groupeta=2 -----

Variable	Sum
Obs1	19.000000
Expl	16.8507484
Obs2	6.000000
Exp2	8.8663366
Obs3	9.000000
Exp3	7.9566853
Obs4	10.000000
Exp4	10.3262297

----- groupeta=3 -----

Variable	Sum
Obs1	24.0000000
Exp1	25.3206838
Obs2	20.0000000
Exp2	16.5131673
Obs3	15.0000000
Exp3	17.2701098
Obs4	27.0000000
Exp4	26.8960391

----- groupeta=4 -----

Variable	Sum
Obs1	13.0000000
Exp1	16.8294428
Obs2	13.0000000
Exp2	13.5552428
Obs3	17.0000000
Exp3	17.1356130
Obs4	40.0000000
Exp4	35.4797013

----- groupeta=5 -----

Variable	Sum
Obs1	11.000000
Exp1	6.7575371
Obs2	5.000000
Exp2	6.4543096
Obs3	11.000000
Exp3	9.8836514
Obs4	27.000000
Exp4	30.9045018

Goodness-of-fit for the four category model  
 Observed and Expected Numbers of patients in each GOS Category  
 in each Group

GroupGS		Category								Total	
		Good		Moderate		Severe		Veg/Dead			
		O	E	O	E	O	E	O	E	O	E
> 0.65		46	46.9	13	11.8	8	7.7	7	7.6	74	74.0
> 0.15 to <= 0.65		19	16.9	6	8.9	9	8.0	10	10.3	44	44.0
> -0.35 to <= 0.15		24	25.3	20	16.5	15	17.3	27	26.9	86	86.0
> -0.85 to <= -0.35		13	16.8	13	13.6	17	17.1	40	35.5	83	83.0
<= -0.85		11	6.8	5	6.5	11	9.9	27	30.9	54	54.0
Total		113	113.0	57	57.0	60	60.0	111	111.0	341	341.0

$$\chi^2 = \sum (O_{ks} - E_{ks})^2 / E_{ks} = 7.731$$

df = no. of cells – no. of parameters – no. of constraints

$$= (s \text{ groups} \times k \text{ categories})$$

$$- (q \text{ explanatory terms} + \text{no. of intercepts})$$

$$- (s \text{ groups})$$

$$= 20 - (4 + 3) - 5$$

$$= 8$$

$$\text{c.f. } \chi^2_8, \quad p = 0.46$$

(Ashby, Pocock and Shaper, 1986)

## **S6.4 To fit stratified proportional odds model using SAS PROC NL MIXED**

\* Read in grouped data from Alzheimer's disease example \*;

```
data cgic;
input study treat cgic5 count;
cards;
1 1 1 4
1 1 2 23
1 1 3 45
1 1 4 22
1 1 5 2
1 0 1 2
1 0 2 22
1 0 3 54
1 0 4 29
1 0 5 3
2 1 1 14
2 1 2 119
2 1 3 180
2 1 4 54
2 1 5 6
2 0 1 1
2 0 2 22
2 0 3 35
2 0 4 11
2 0 5 3
3 1 1 13
3 1 2 20
3 1 3 24
3 1 4 10
3 1 5 1
3 0 1 7
3 0 2 16
3 0 3 17
3 0 4 10
3 0 5 3
4 1 1 21
4 1 2 106
4 1 3 175
4 1 4 62
4 1 5 17
4 0 1 8
4 0 2 24
4 0 3 73
4 0 4 52
4 0 5 13
5 1 1 3
5 1 2 14
5 1 3 19
5 1 4 3
5 1 5 0
5 0 1 2
5 0 2 13
```

```

5 0 3 18
5 0 4 7
5 0 5 1
;
run;

* Macro for creating intercept terms in stratified model *;

%macro alpha(i,k);
  %if &k=1 %then a&i.1;
  %if &k=2 %then a&i.1 + a&i.2;
  %if &k=3 %then a&i.1 + a&i.2 + a&i.3;
  %if &k=4 %then a&i.1 + a&i.2 + a&i.3 + a&i.4;
%mend alpha;

* Fit proportional odds model for more favourable outcome with *
* treatment, stratified by study                         *;

* Use PROC NLMIXED with study and treatment as fixed effects *;

proc nlmixed data=cgic;
  parms a11 a12 a13 a14 a21 a22 a23 a24 a31 a32 a33 a34
        a41 a42 a43 a44 a51 a52 a53 a54 = 1, betal = 0;
  bounds a12 a13 a14 a22 a23 a24 a32 a33 a34 a42 a43 a44
        a52 a53 a54 > 0;

  eta = betal*treat;

  if study = 1 and cgic5 = 1 then do;
    qk = 1/(1+exp(-(%alpha(1,1))-eta));
    qk_1 = 0;
  end;
  if study = 1 and cgic5 = 2 then do;
    qk = 1/(1+exp(-(%alpha(1,2))-eta));
    qk_1 = 1/(1+exp(-(%alpha(1,1))-eta));
  end;
  if study = 1 and cgic5 = 3 then do;
    qk = 1/(1+exp(-(%alpha(1,3))-eta));
    qk_1 = 1/(1+exp(-(%alpha(1,2))-eta));
  end;
  if study = 1 and cgic5 = 4 then do;
    qk = 1/(1+exp(-(%alpha(1,4))-eta));
    qk_1 = 1/(1+exp(-(%alpha(1,3))-eta));
  end;
  if study = 1 and cgic5 = 5 then do;
    qk = 1;
    qk_1 = 1/(1+exp(-(%alpha(1,4))-eta));
  end;
  if study = 2 and cgic5 = 1 then do;
    qk = 1/(1+exp(-(%alpha(2,1))-eta));
    qk_1 = 0;
  end;
  if study = 2 and cgic5 = 2 then do;
    qk = 1/(1+exp(-(%alpha(2,2))-eta));
    qk_1 = 1/(1+exp(-(%alpha(2,1))-eta));
  end;

```

```

if study = 2 and cgic5 = 3 then do;
  qk = 1/(1+exp(-(%alpha(2,3))-eta));
  qk_1 = 1/(1+exp(-(%alpha(2,2))-eta));
end;
if study = 2 and cgic5 = 4 then do;
  qk = 1/(1+exp(-(%alpha(2,4))-eta));
  qk_1 = 1/(1+exp(-(%alpha(2,3))-eta));
end;
if study = 2 and cgic5 = 5 then do;
  qk = 1;
  qk_1 = 1/(1+exp(-(%alpha(2,4))-eta));
end;
if study = 3 and cgic5 = 1 then do;
  qk = 1/(1+exp(-(%alpha(3,1))-eta));
  qk_1 = 0;
end;
if study = 3 and cgic5 = 2 then do;
  qk = 1/(1+exp(-(%alpha(3,2))-eta));
  qk_1 = 1/(1+exp(-(%alpha(3,1))-eta));
end;
if study = 3 and cgic5 = 3 then do;
  qk = 1/(1+exp(-(%alpha(3,3))-eta));
  qk_1 = 1/(1+exp(-(%alpha(3,2))-eta));
end;
if study = 3 and cgic5 = 4 then do;
  qk = 1/(1+exp(-(%alpha(3,4))-eta));
  qk_1 = 1/(1+exp(-(%alpha(3,3))-eta));
end;
if study = 3 and cgic5 = 5 then do;
  qk = 1;
  qk_1 = 1/(1+exp(-(%alpha(3,4))-eta));
end;
if study = 4 and cgic5 = 1 then do;
  qk = 1/(1+exp(-(%alpha(4,1))-eta));
  qk_1 = 0;
end;
if study = 4 and cgic5 = 2 then do;
  qk = 1/(1+exp(-(%alpha(4,2))-eta));
  qk_1 = 1/(1+exp(-(%alpha(4,1))-eta));
end;
if study = 4 and cgic5 = 3 then do;
  qk = 1/(1+exp(-(%alpha(4,3))-eta));
  qk_1 = 1/(1+exp(-(%alpha(4,2))-eta));
end;
if study = 4 and cgic5 = 4 then do;
  qk = 1/(1+exp(-(%alpha(4,4))-eta));
  qk_1 = 1/(1+exp(-(%alpha(4,3))-eta));
end;
if study = 4 and cgic5 = 5 then do;
  qk = 1;
  qk_1 = 1/(1+exp(-(%alpha(4,4))-eta));
end;
if study = 5 and cgic5 = 1 then do;
  qk = 1/(1+exp(-(%alpha(5,1))-eta));
  qk_1 = 0;
end;

```

```

if study = 5 and cgic5 = 2 then do;
  qk = 1/(1+exp(-(%alpha(5,2))-eta));
  qk_1 = 1/(1+exp(-(%alpha(5,1))-eta));
end;
if study = 5 and cgic5 = 3 then do;
  qk = 1/(1+exp(-(%alpha(5,3))-eta));
  qk_1 = 1/(1+exp(-(%alpha(5,2))-eta));
end;
if study = 5 and cgic5 = 4 then do;
  qk = 1/(1+exp(-(%alpha(5,4))-eta));
  qk_1 = 1/(1+exp(-(%alpha(5,3))-eta));
end;
if study = 5 and cgic5 = 5 then do;
  qk = 1;
  qk_1 = 1/(1+exp(-(%alpha(5,4))-eta));
end;

p=qk-qk_1;

if p>1e-8 then ll=log(p);
else ll=-1e100;

model cgic5 ~ general(ll);
replicate count;
run;

```

## Proportional odds model for more favourable outcome with treatment, stratified by study

The NL MIXED Procedure

### Specifications

Data Set	WORK.CGIC
Dependent Variable	cgic5
Distribution for Dependent Variable	General
Replicate Variable	count
Optimization Technique	Dual Quasi-Newton
Integration Method	None

### Dimensions

Observations Used	49
Observations Not Used	1
Total Observations	50
Parameters	21

### Parameters

a11	a12	a13	a14	a21	a22	a23	a24
1	1	1	1	1	1	1	1

### Parameters

a31	a32	a33	a34	a41	a42	a43	a44
1	1	1	1	1	1	1	1

Parameters					
a51	a52	a53	a54	beta1	NegLogLike
1	1	1	1	0	3542.5429

Iteration History					
Iter	Calls	NegLogLike	Diff	MaxGrad	Slope
1	3	2524.04195	1018.501	282.1493	-9029.73
2	4	2339.70038	184.3416	77.06235	-290.422
3	6	2148.73504	190.9653	81.13803	-158.602
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
46	76	1779.83463	0.000045	0.023433	-0.00023
47	77	1779.83456	0.00007	0.019578	-0.00015
48	79	1779.83456	7.123E-6	0.023019	-0.00001

NOTE: GCONV convergence criterion satisfied.

#### Fit Statistics

<b>-2 Log Likelihood</b>	<b>3559.7</b>
AIC (smaller is better)	3601.7
AICC (smaller is better)	3635.9
BIC (smaller is better)	3641.4

#### Parameter Estimates

Parameter	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower
a11	-3.7588	0.4182	49	-8.99	<.0001	0.05	-4.5991
a12	2.4037	0.3966	49	6.06	<.0001	0.05	1.6067
a13	2.1187	0.1830	49	11.58	<.0001	0.05	1.7509
a14	2.7218	0.4407	49	6.18	<.0001	0.05	1.8361
a21	-3.7880	0.2802	49	-13.52	<.0001	0.05	-4.3511
a22	2.7446	0.2563	49	10.71	<.0001	0.05	2.2296
a23	2.2388	0.1339	49	16.72	<.0001	0.05	1.9697
a24	2.2737	0.3199	49	7.11	<.0001	0.05	1.6309
a31	-1.9186	0.2548	49	-7.53	<.0001	0.05	-2.4307
a32	1.4804	0.2257	49	6.56	<.0001	0.05	1.0269
a33	1.5588	0.2180	49	7.15	<.0001	0.05	1.1206
a34	1.9931	0.4752	49	4.19	0.0001	0.05	1.0381
a41	-3.2719	0.2096	49	-15.61	<.0001	0.05	-3.6930
a42	2.0010	0.1793	49	11.16	<.0001	0.05	1.6406
a43	1.9762	0.1083	49	18.24	<.0001	0.05	1.7585
a44	1.8347	0.1741	49	10.54	<.0001	0.05	1.4849
a51	-2.9833	0.4672	49	-6.39	<.0001	0.05	-3.9222
a52	2.3166	0.4475	49	5.18	<.0001	0.05	1.4173
a53	2.2695	0.3333	49	6.81	<.0001	0.05	1.5996
a54	2.5480	0.9674	49	2.63	0.0113	0.05	0.6040
<b>beta1</b>	$\hat{\theta}$	<b>0.5048</b>	<b>0.1121</b>	49	4.50	<.0001	0.05
							0.2795

$\hat{\theta}$  is estimate of the log odds of a more favourable outcome with Tacrine compared to placebo, stratified by study.

## **S6.5 Analysis of grouped ordinal data using R**

```
# Read grouped data from severe head injury study (example 1) into a data frame
head1 <- data.frame(GCSENTRY=c(1,1,1,1,2,2,2,2,2),
                      GOS=c(1,2,3,4,5,1,2,3,4,5),
                      FREQUENCY=c(73,55,79,37,358,219,118,66,10,92))

# Convert ordinal outcome variable from numeric variable to factor variable
# with 5 (Dead) as the first level and 1 (Good) as the last level so that
# lrm function will model cumulative probabilities of more favourable outcome

head1$GOS <- factor(head1$GOS, levels=c('5','4','3','2','1'),
                      labels=c('Dead','Vegetative','Severe Dis','Mod Dis','Good'))

# Convert categorical predictor from numeric variable to factor variable

head1$GCSENTRY <- factor(head1$GCSENTRY, levels=c('1','2'),
                           labels=c('GCS 3-5','GCS 6-8'))

# Load rms package

library(rms)

# Fit proportional odds model for more favourable outcome with GCS at entry

pom.fit1 <- lrm(GOS ~ GCSENTRY, data=head1, weight=FREQUENCY)
print(pom.fit1)
```

The **weight=** option is used because the data are in summarised form rather than with a row for each individual.

```
# Obtain linear predictors, predicted cumulative probabilities, and
# predicted probabilities

# Linear predictors for log odds of GOS = 'Good', GOS = 'Mod Dis' or better,
# GOS = 'Severe Dis' or better, and GOS = 'Vegetative' or better are derived
# using fourth, third, second, and first intercepts respectively

fitted1 <- cbind(head1,
                  XBETA1=predict(pom.fit1, head1, type='lp', kint=4),
                  XBETA2=predict(pom.fit1, head1, type='lp', kint=3),
                  XBETA3=predict(pom.fit1, head1, type='lp', kint=2),
                  XBETA4=predict(pom.fit1, head1, type='lp', kint=1),
                  predict(pom.fit1, head1, type='fitted'),
                  predict(pom.fit1, head1, type='fitted.ind'))

print(fitted1[,c('GCSENTRY','GOS','FREQUENCY','XBETA1','XBETA2','XBETA3',
               'XBETA4')])
print(fitted1[,c('GCSENTRY','y>=Good','y>=Mod Dis','y>=Severe Dis',
               'y>=Vegetative')])
print(fitted1[,c('GCSENTRY','GOS=Good','GOS=Mod Dis','GOS=Severe Dis',
               'GOS=Vegetative','GOS=Dead')])
```

```

# Calculate expected values for each GOS category by GCS at entry

expected <- data.frame(GCSENTRY=head1$GCSENTRY,
                        E_Good=fitted1$FREQUENCY*fitted1$"GOS=Good",
                        E_Mod_Dis=fitted1$FREQUENCY*fitted1$"GOS=Mod Dis",
                        E_Severe_Dis=fitted1$FREQUENCY*fitted1$"GOS=Severe Dis",
                        E_Vegetative=fitted1$FREQUENCY*fitted1$"GOS=Vegetative",
                        E_Dead=fitted1$FREQUENCY*fitted1$"GOS=Dead")

EXPECTED <- c(sum(expected[expected$GCSENTRY=='GCS 3-5','E_Good']),
              sum(expected[expected$GCSENTRY=='GCS 3-5','E_Mod_Dis']),
              sum(expected[expected$GCSENTRY=='GCS 3-5','E_Severe_Dis']),
              sum(expected[expected$GCSENTRY=='GCS 3-5','E_Vegetative']),
              sum(expected[expected$GCSENTRY=='GCS 3-5','E_Dead']),
              sum(expected[expected$GCSENTRY=='GCS 6-8','E_Good']),
              sum(expected[expected$GCSENTRY=='GCS 6-8','E_Mod_Dis']),
              sum(expected[expected$GCSENTRY=='GCS 6-8','E_Severe_Dis']),
              sum(expected[expected$GCSENTRY=='GCS 6-8','E_Vegetative']),
              sum(expected[expected$GCSENTRY=='GCS 6-8','E_Dead']))

obsexp <- data.frame(head1, EXPECTED)

print(obsexp)

```

## Proportional Odds Model

Logistic Regression Model

```
lrm(formula = GOS ~ GCSENTRY, data = head1, weights = FREQUENCY)
```

Frequencies of Responses

	Dead	Vegetative	Severe	Dis	Mod	Dis	Good
	2	2	2	2			2

Sum of Weights by Response Category

	0	1	2	3	4
	450	47	145	173	292

	Model Likelihood	Discrimination	Rank Discrim.
	Ratio Test	Indexes	Indexes
Obs	10	R2	C
Sum of weights	1107	d.f.	Dxy
max  deriv	1e-07	Pr(> chi2) <0.0001	gamma
		gr	tau-a
		gp	
		Brier	0.681
		0.228	0.361
		1.055	0.658
		2.871	0.261
		0.240	
		0.196	

	Coef	S.E.	Wald Z	Pr(> Z )
y>=Vegetative	$\hat{\alpha}_4$	-0.3861	0.0816	-4.73 <0.0001
y>=Severe Dis	$\hat{\alpha}_3$	-0.6006	0.0831	-7.23 <0.0001
y>=Mod Dis	$\hat{\alpha}_2$	-1.2698	0.0915	-13.88 <0.0001
y>=Good	$\hat{\alpha}_1$	-2.1223	0.1051	-20.19 <0.0001
GCSENTRY=GCS 6-8	$\hat{\beta}$	1.8985	0.1214	15.64 <0.0001

## Linear Predictors

	GCSENTRY	GOS	FREQUENCY	XBETA1	XBETA2	XBETA3	XBETA4
1	<b>GCS 3-5</b>	Good	73	<b>-2.1222861</b>	<b>-1.2698372</b>	<b>-0.6006347</b>	<b>-0.3861009</b>
2	GCS 3-5	Mod Dis	55	-2.1222861	-1.2698372	-0.6006347	-0.3861009
3	GCS 3-5	Severe Dis	79	-2.1222861	-1.2698372	-0.6006347	-0.3861009
4	GCS 3-5	Vegetative	37	-2.1222861	-1.2698372	-0.6006347	-0.3861009
5	GCS 3-5	Dead	358	-2.1222861	-1.2698372	-0.6006347	-0.3861009
6	GCS 6-8	Good	219	-0.2238070	0.6286419	1.2978444	1.5123782
7	GCS 6-8	Mod Dis	118	-0.2238070	0.6286419	1.2978444	1.5123782
8	GCS 6-8	Severe Dis	66	-0.2238070	0.6286419	1.2978444	1.5123782
9	GCS 6-8	Vegetative	10	-0.2238070	0.6286419	1.2978444	1.5123782
10	<b>GCS 6-8</b>	Dead	92	<b>-0.2238070</b>	<b>0.6286419</b>	<b>1.2978444</b>	<b>1.5123782</b>

## Predicted Cumulative Probabilities

	GCSENTRY	y>=Good	y>=Mod Dis	y>=Severe Dis	y>=Vegetative
1	<b>GCS 3-5</b>	<b>0.1069495</b>	<b>0.2192851</b>	<b>0.3541985</b>	<b>0.4046563</b>
2	GCS 3-5	0.1069495	0.2192851	0.3541985	0.4046563
3	GCS 3-5	0.1069495	0.2192851	0.3541985	0.4046563
4	GCS 3-5	0.1069495	0.2192851	0.3541985	0.4046563
5	GCS 3-5	0.1069495	0.2192851	0.3541985	0.4046563
6	GCS 6-8	0.4442806	0.6521815	0.7854720	0.8194134
7	GCS 6-8	0.4442806	0.6521815	0.7854720	0.8194134
8	GCS 6-8	0.4442806	0.6521815	0.7854720	0.8194134
9	GCS 6-8	0.4442806	0.6521815	0.7854720	0.8194134
10	<b>GCS 6-8</b>	<b>0.4442806</b>	<b>0.6521815</b>	<b>0.7854720</b>	<b>0.8194134</b>

## Predicted Probabilities

	GCSENTRY	GOS=Good	GOS=Mod Dis	GOS=Severe Dis	GOS=Vegetative	GOS=Dead
1	<b>GCS 3-5</b>	<b>0.1069495</b>	<b>0.1123356</b>	<b>0.1349134</b>	<b>0.05045776</b>	<b>0.5953437</b>
2	GCS 3-5	0.1069495	0.1123356	0.1349134	0.05045776	0.5953437
3	GCS 3-5	0.1069495	0.1123356	0.1349134	0.05045776	0.5953437
4	GCS 3-5	0.1069495	0.1123356	0.1349134	0.05045776	0.5953437
5	GCS 3-5	0.1069495	0.1123356	0.1349134	0.05045776	0.5953437
6	GCS 6-8	0.4442806	0.2079008	0.1332905	0.03394140	0.1805866
7	GCS 6-8	0.4442806	0.2079008	0.1332905	0.03394140	0.1805866
8	GCS 6-8	0.4442806	0.2079008	0.1332905	0.03394140	0.1805866
9	GCS 6-8	0.4442806	0.2079008	0.1332905	0.03394140	0.1805866
10	<b>GCS 6-8</b>	<b>0.4442806</b>	<b>0.2079008</b>	<b>0.1332905</b>	<b>0.03394140</b>	<b>0.1805866</b>

## Observed and Expected Frequencies

	GCSENTRY	GOS	FREQUENCY	EXPECTED
1	GCS 3-5	Good	73	64.38362
2	GCS 3-5	Mod Dis	55	67.62603
3	GCS 3-5	Severe Dis	79	81.21786
4	GCS 3-5	Vegetative	37	30.37557
5	GCS 3-5	Dead	358	358.39692
6	GCS 6-8	Good	219	224.36173
7	GCS 6-8	Mod Dis	118	104.98991
8	GCS 6-8	Severe Dis	66	67.31172
9	GCS 6-8	Vegetative	10	17.14041
10	GCS 6-8	Dead	92	91.19624

## **S6.6 Analysis of ungrouped ordinal data using R**

Data from head injury study (example 2) in head2 data frame. See supplement to session 2 for details of these data.

```
# Load saved workspace which contains data frame with ungrouped data from
# head injury study (example 2)

load('head2.RData')

# Convert ordinal outcome variable from numeric variable to factor variable
# with 4 (Veg/Dead) as the first level and 1 (Good) as the last level so that
# lrm function will model cumulative probabilities of more favourable outcome

head2$GOS4 <- factor(head2$GOS4, levels=c('4','3','2','1'))

# Convert categorical predictors from numeric variables to factor variables

head2$GCSMOTOR <- factor(head2$GCSMOTOR, levels=c('1','2','3'))
head2$TREAT <- factor(head2$TREAT, levels=c('0','1'))

# Load rms package

library(rms)

# Fit proportional odds model for more favourable outcome with age,
# GCS motor score and treatment

pom.fit2 <- lrm(GOS4 ~ AGE + GCSMOTOR + TREAT, data=head2)
print(pom.fit2)

# Obtain linear predictors, predicted cumulative probabilities, and
# predicted probabilities

# Linear predictors for log odds of GOS4 = 1 or better, GOS4 = 2 or better,
# and GOS4 = 3 or better are derived using third, second, and first intercepts
# respectively

fitted2 <- cbind(head2,
                  XBETA1=predict(pom.fit2, head2, type='lp', kint=3),
                  XBETA2=predict(pom.fit2, head2, type='lp', kint=2),
                  XBETA3=predict(pom.fit2, head2, type='lp', kint=1),
                  predict(pom.fit2, head2, type='fitted'),
                  predict(pom.fit2, head2, type='fitted.ind'))

print(fitted2[,c('PATIENT','AGE','GCSMOTOR','TREAT','GOS4','XBETA1','XBETA2',
'XBETA3')], row.names=FALSE)

# Calculate individual linear predictor for each patient

fitted2$ETA <- fitted2$XBETA1 - pom.fit2$coefficients['y>=1']

print(fitted2[,c('PATIENT','AGE','GCSMOTOR','TREAT','GOS4','ETA')], row.names=FALSE)
```

```

# Classify each patient into one of five groups based on value of individual
# linear predictor

fitted2$GROUPETA <- 6 - cut(fitted2$ETA, breaks=c(-Inf,-0.85,-0.35,0.15,
0.65,Inf), labels=FALSE)

# Calculate observed frequencies for each GOS4 category by individual linear
# predictor group

OBS1 <- rowsum(as.numeric(fitted2$GOS4==1), fitted2$GROUPETA)
OBS2 <- rowsum(as.numeric(fitted2$GOS4==2), fitted2$GROUPETA)
OBS3 <- rowsum(as.numeric(fitted2$GOS4==3), fitted2$GROUPETA)
OBS4 <- rowsum(as.numeric(fitted2$GOS4==4), fitted2$GROUPETA)

# Calculate expected frequencies for each GOS4 category by individual linear
# predictor group

EXP1 <- rowsum(fitted2$'GOS4=1', fitted2$GROUPETA)
EXP2 <- rowsum(fitted2$'GOS4=2', fitted2$GROUPETA)
EXP3 <- rowsum(fitted2$'GOS4=3', fitted2$GROUPETA)
EXP4 <- rowsum(fitted2$'GOS4=4', fitted2$GROUPETA)

GROUPETA <- c(1:5)
GROUPETA <- factor(GROUPETA, levels=c('1','2','3','4','5'),
labels=c('> 0.65','> 0.15 to <= 0.65','>-0.35 to <= 0.15',
'>-0.85 to <=-0.35','<=-0.85')))

obsexp <- data.frame(GROUPETA,OBS1,EXP1,OBS2,EXP2,OBS3,EXP3,OBS4,EXP4)
print(obsexp, row.names=FALSE)

```

## Proportional Odds Model

Logistic Regression Model

```
lrm(formula = GOS4 ~ AGE + GCSMOTOR + TREAT, data = head2)
```

Frequencies of Responses

4	3	2	1
111	60	57	113

	Model Likelihood	Discrimination		Rank Discrim.				
	Ratio Test	Indexes	Indexes	Indexes	Indexes			
Obs	341	LR	chi2	68.02	R2	0.194	C	0.682
max  deriv	7e-10	d.f.		4	g	0.987	Dxy	0.365
		Pr(> chi2)	<0.0001		gr	2.683	gamma	0.367
					gp	0.216	tau-a	0.265
					Brier	0.213		

	Coef	S.E.	Wald Z	Pr(> Z )	
y>=3	$\hat{\alpha}_3$	<b>0.8462</b>	0.2918	2.90	0.0037
y>=2	$\hat{\alpha}_2$	<b>0.0012</b>	0.2873	0.00	0.9967
y>=1	$\hat{\alpha}_1$	<b>-0.8217</b>	0.2919	-2.82	0.0049
AGE	$\hat{\beta}_1$	<b>-0.0247</b>	0.0069	-3.56	0.0004
GCSMOTOR=2	$\hat{\beta}_2$	<b>0.5058</b>	0.2338	2.16	0.0305
GCSMOTOR=3	$\hat{\beta}_3$	<b>1.9026</b>	0.2803	6.79	<0.0001
TREAT=1	$\hat{\beta}_4$	<b>0.6019</b>	0.2056	2.93	0.0034

## Linear Predictors

PATIENT	AGE	GCSMOTOR	TREAT	GOS4	XBETA1	XBETA2	XBETA3
1	66	1	0	1	-2.449087433	-1.6262100113	-0.781243041
2	63	1	1	1	-1.773176425	-0.9502990033	-0.105332033
3	58	1	1	1	-1.649888539	-0.8270111168	0.017955854
4	54	1	0	1	-2.153196506	-1.3303190836	-0.485352113
5	51	1	1	1	-1.477285498	-0.6544080756	0.190558895
6	49	1	0	1	-2.029908619	-1.2070311971	-0.362064227
7	49	1	1	1	-1.427970343	-0.6050929210	0.239874049
8	46	1	0	1	-1.955935887	-1.1330584651	-0.288091495
9	46	1	1	1	-1.353997611	-0.5311201891	0.313846781
10	43	1	0	1	-1.881963155	-1.0590857332	-0.214118763

etc.

## Individual Linear Predictor

PATIENT	AGE	GCSMOTOR	TREAT	GOS4	ETA
1	66	1	0	1	-1.627400102
2	63	1	1	1	-0.951489094
3	58	1	1	1	-0.828201208
4	54	1	0	1	-1.331509175
5	51	1	1	1	-0.655598167
6	49	1	0	1	-1.208221288
7	49	1	1	1	-0.606283012
8	46	1	0	1	-1.134248556
9	46	1	1	1	-0.532310280
10	43	1	0	1	-1.060275824

etc.

## Observed and Expected Frequencies

GROUPETA	OBS1	EXP1	OBS2	EXP2	OBS3	EXP3	OBS4	EXP4
> 0.65	46	46.854106	13	11.786505	8	7.748265	7	7.611123
> 0.15 to <= 0.65	19	16.850622	6	8.866377	9	7.956749	10	10.326252
>-0.35 to <= 0.15	24	25.320507	20	16.513212	15	17.270218	27	26.896063
>-0.85 to <=-0.35	13	16.829245	13	13.555228	17	17.135697	40	35.479830
<=-0.85	11	6.757345	5	6.454214	11	9.883618	27	30.904824

## **S6.7 Stratified proportional odds model using R**

```
# Read grouped data from Alzheimer's disease example into a data frame

cgic <- expand.grid(CGIC5=c(1:5), TREAT=c(1,0), STUDY=c(1:5))
cgic$COUNT <- c(4,23,45,22,2,
               2,22,54,29,3,
               14,119,180,54,6,
               1,22,35,11,3,
               13,20,24,10,1,
               7,16,17,10,3,
               21,106,175,62,17,
               8,24,73,52,13,
               3,14,19,3,0,
               2,13,18,7,1)

# Convert ordinal outcome variable from numeric variable to factor variable with
# 1 (Very much or much improved) as first and 5 (Very much or much worse) as
# last level so that clm function will model cumulative probabilities of more
# favourable outcome

cgic$CGIC5 <- factor(cgic$CGIC5, levels=c('1','2','3','4','5'))

# Convert stratification variable from numeric variable to factor variable

cgic$STUDY <- factor(cgic$STUDY, levels=c('1','2','3','4','5'))

# Convert categorical predictor from numeric variable to factor variable

cgic$TREAT <- factor(cgic$TREAT, levels=c('0','1'),
                      labels=c('Placebo','Tacrine'))

# load ordinal package

library (ordinal)

# Fit proportional odds model for more favourable outcome with treatment,
# stratified by study

clm.fit1 <- clm(CGIC5 ~ TREAT, nominal = ~ STUDY, data=cgic, weights=COUNT,
link='logistic')
summary(clm.fit1)

# Fit model for more favourable outcome stratified by study but without
# treatment

clm.fit2 <- clm(CGIC5 ~ 1, nominal = ~ STUDY, data=cgic, weights=COUNT,
link='logistic')
summary(clm.fit2)

# Likelihood ratio test for treatment, stratified by study, from taking
# difference between -2 Log L for last two clm function calls

anova(clm.fit2, clm.fit1)
```

## Proportional odds model for more favourable outcome with treatment, stratified by study

```

Call:
clm(location = CGIC5 ~ TREAT, nominal = ~STUDY, data = cgic,
     weights = COUNT, link = "logistic")

Location coefficients:
              Estimate Std. Error z value Pr(>|z|)
TREATTacrine   -0.5048    0.1121   -4.5031 6.6964e-06

No scale coefficients

Threshold coefficients:
                Estimate Std. Error z value
1 | 2.(Intercept) -3.7624    0.4189  -8.9821
2 | 3.(Intercept) -1.3553    0.1716  -7.8996
3 | 4.(Intercept)  0.7637    0.1644   4.6450
4 | 5.(Intercept)  3.4810    0.4552   7.6481
1 | 2.STUDY2      -0.0258    0.4923  -0.0524
2 | 3.STUDY2      0.3119    0.1944   1.6040
3 | 4.STUDY2      0.4318    0.2073   2.0832
4 | 5.STUDY2      -0.0131    0.5663  -0.0231
1 | 2.STUDY3      1.8436    0.4819   3.8255
2 | 3.STUDY3      0.9171    0.2450   3.7435
3 | 4.STUDY3      0.3567    0.2780   1.2832
4 | 5.STUDY3      -0.3684    0.6814  -0.5406
1 | 2.STUDY4      0.4904    0.4572   1.0726
2 | 3.STUDY4      0.0844    0.1896   0.4451
3 | 4.STUDY4      -0.0584    0.1868  -0.3125
4 | 5.STUDY4      -0.9410    0.4910  -1.9166
1 | 2.STUDY5      0.7808    0.6211   1.2571
2 | 3.STUDY5      0.6889    0.2812   2.4498
3 | 4.STUDY5      0.8384    0.3616   2.3183
4 | 5.STUDY5      0.6702    1.1038   0.6072

log-likelihood: -1779.834
AIC: 3601.669
Condition number of Hessian: 969.5578

```

Note: The clm function interprets a response variable with more than two categories as an ordinal response and models the cumulative probabilities of lower ordered values. So in this example to model the cumulative probabilities of more favourable outcomes the five levels of CGIC5 have been ordered with ‘Very much or much improved’ as the first level and ‘Very much or much worse’ as the last level. This ordering is the opposite of that required by the lrm function in the rms package but is the same as that required by PROC LOGISTIC and PROC GENMOD in SAS. Since the clm function can fit a variety of cumulative link models the link=‘logistic’ option is used to specify that a proportional odds model or stratified proportional odds model should be fitted.

In models fitted by the clm function the linear predictor has the following form:  $\alpha_{sk} - \eta(z_i)$ . This has  $- \eta(z_i)$  rather than  $+ \eta(z_i)$  as used in the lrm function in R and the various procedures in SAS. Therefore estimates of the regression coefficients ( $\hat{\beta}$ s) using the clm function will have the opposite sign. So in this example the estimate of the log odds of a more favourable outcome with Tacrine compared to placebo, stratified by study, is:  $\hat{\theta} = -\hat{\beta} = 0.5048$

## Model for more favourable outcome stratified by study but without treatment

```
Call:  
clm(location = CGIC5 ~ 1, nominal = ~STUDY, data = cgic, weights = COUNT,  
link = "logistic")  
  
No location coefficients  
  
No scale coefficients  
  
Threshold coefficients:  
Estimate Std. Error z value  
1 | 2.(Intercept) -3.5066 0.4143 -8.4633  
2 | 3.(Intercept) -1.1116 0.1614 -6.8860  
3 | 4.(Intercept) 0.9853 0.1566 6.2917  
4 | 5.(Intercept) 3.6939 0.4527 8.1589  
1 | 2.STUDY2 0.1508 0.4906 0.3074  
2 | 3.STUDY2 0.4950 0.1896 2.6116  
3 | 4.STUDY2 0.6269 0.2018 3.1060  
4 | 5.STUDY2 0.1866 0.5643 0.3306  
1 | 2.STUDY3 1.8872 0.4812 3.9217  
2 | 3.STUDY3 0.9626 0.2435 3.9527  
3 | 4.STUDY3 0.4114 0.2766 1.4873  
4 | 5.STUDY3 -0.3180 0.6808 -0.4671  
1 | 2.STUDY4 0.6162 0.4561 1.3509  
2 | 3.STUDY4 0.2092 0.1868 1.1200  
3 | 4.STUDY4 0.0537 0.1842 0.2916  
4 | 5.STUDY4 -0.8393 0.4901 -1.7124  
1 | 2.STUDY5 0.7985 0.6205 1.2869  
2 | 3.STUDY5 0.7061 0.2795 2.5261  
3 | 4.STUDY5 0.8509 0.3605 2.3607  
4 | 5.STUDY5 0.6756 1.1035 0.6122  
  
log-likelihood: -1790.047  
AIC: 3620.095  
Condition number of Hessian: 937.9847
```

## Likelihood ratio test for treatment, stratified by study

Likelihood ratio tests of cumulative link models

```
Response: CGIC5  
Model Resid. df -2logLik Test Df LR stat. Pr(Chi)  
1 1 | STUDY 1383 3580.095  
2 TREAT | STUDY 1382 3559.669 1 vs 2 1 20.42567 6.199266e-06
```