Two-level Poisson model

Contents

3.1 Two-level models for count outcomes from ASPART data

3.1.1 The data

The data for this example are taken from a paper by McKnight and Van Den Eeden (1993), who reported on the number of headaches in a two treatment, multiple period crossover trial. Specifically, the number of headaches per week was repeatedly measured for 27 patients. Following a seven day placebo run-in period, subjects received either aspartame or placebo in four seven-day treatment periods according to the double-blind crossover treatment design. Each treatment period was separated by a washout day. The sample size is 122. Data for the first 10 observations of all the variables used in this section are shown below in the form of a SuperMix spreadsheet window for **aspart.ss3**.

aspart.ss3

ID | Apply

	(A)_ID	(B)_Headac	(C)_Period1	(D)_Period2	(E)_Period3	(F)_Period4	(G)_DrugAsp	(H)_NPerio	(I)_NTDays
1	2.00	0.00	0.00	0.00	0.00	0.00	0.00	3.00	7.00
2	2.00	5.00	1.00	0.00	0.00	0.00	1.00	3.00	7.00
3	2.00	2.00	0.00	1.00	0.00	0.00	0.00	3.00	7.00
4	5.00	3.00	0.00	0.00	0.00	0.00	0.00	5.00	7.00
5	5.00	0.00	1.00	0.00	0.00	0.00	1.00	5.00	7.00
6	5.00	2.00	0.00	1.00	0.00	0.00	0.00	5.00	7.00
7	5.00	0.00	0.00	0.00	1.00	0.00	1.00	5.00	7.00
8	5.00	0.00	0.00	0.00	0.00	1.00	0.00	5.00	7.00
9	13.00	7.00	0.00	0.00	0.00	0.00	0.00	5.00	7.00
10	13.00	7.00	1.00	0.00	0.00	0.00	1.00	5.00	7.00

The variables of interest are:

- ID is the patient ID (27 patients in total).
- Headache is the number of headaches during the week (from 0 to 7).
- Period1 is a period 1 treatment indicator (1 for the first treatment period and 0 otherwise).
- Period2 is a period 2 treatment indicator (1 for the second treatment period and 0 otherwise).
- Period3 is a period 3 treatment indicator (1 for the third treatment period and 0 otherwise).
- Period4 is a period 4 treatment indicator (1 for the fourth treatment period and 0 otherwise).
- DrugAsp indicates the type of drug being used for the treatment, (0 = placebo and 1 = aspartame). 75 observations used placebo and 47 used aspartame.
- Nperiods is the number of periods the individual was observed (from 2 to 5).
- NTDays is the number of treatment days in the period (from 1 to 7).

3.1.2 A 2 level Poisson model with random intercept

3.1.2.1 The model

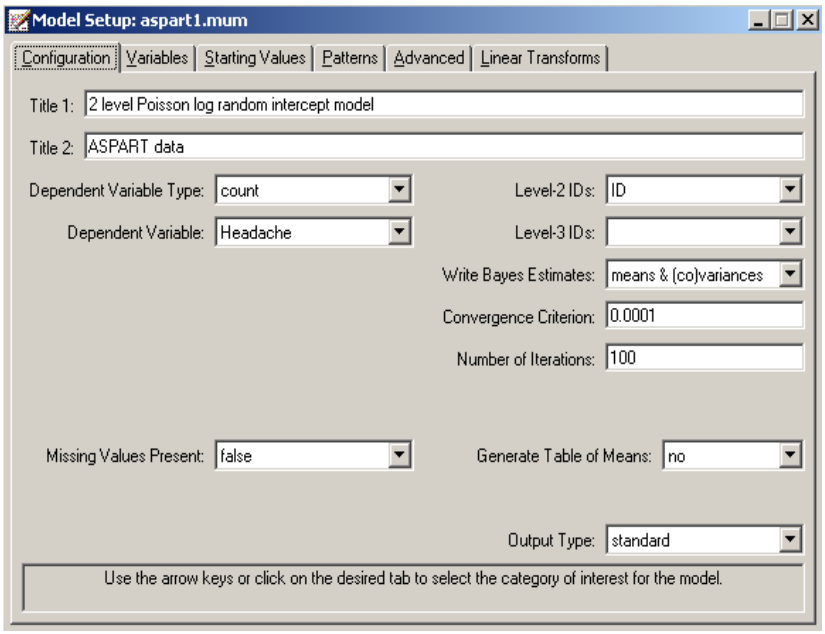
To model the relationship between the number of headaches during the week (Headache) and the treatment indicators (Period1 to Period4) and the type of drug administered (DrugAsp), the following Poisson regression model with a random intercept may be used:

$$\log\left(\lambda_{ij}\right) = \beta_0 + \beta_1 \times \text{Period1}_{ij} + \beta_2 \times \text{Period2}_{ij} + \beta_3 \times \text{Period3}_{ij} + \beta_4 \times \text{Period4}_{ij} + \beta_5 \times \text{DrugAsp}_{ij} + v_{i0}$$

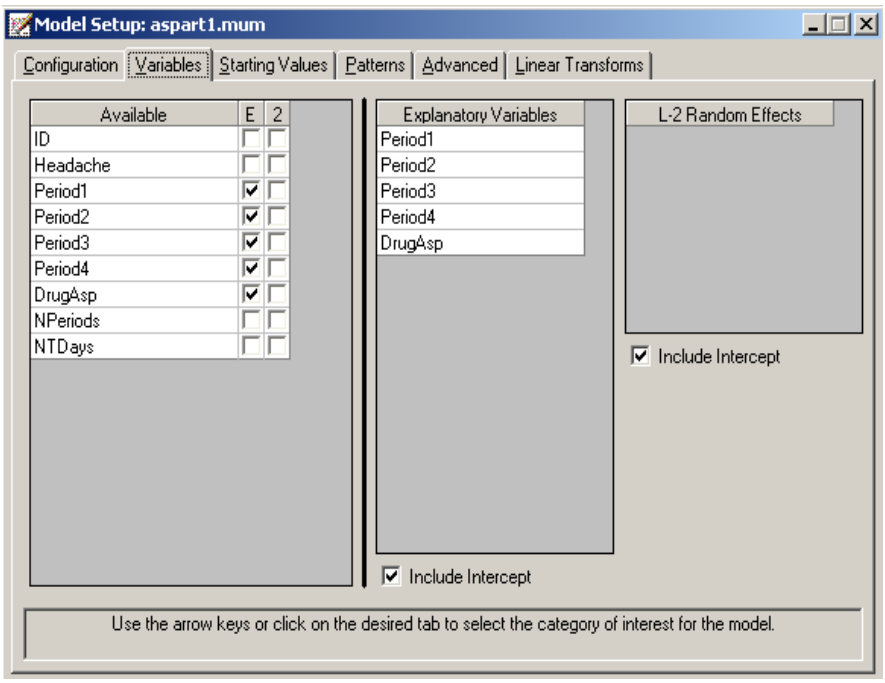
where λ_{ij} denotes the mean number of headaches of patient i for treatment period j; Period1_{ij}, Period2_{ij}, Period3_{ij} and Period4_{ij} denote the values of the dummy variables Period1, Period2, Period3 and Period4 for patient i for treatment period j respectively; DrugAsp_{ij} denotes the value of the DrugAsp for patient i for treatment period j; β_0, β_1, β_2, β_3, β_4 and β_5 denote unknown parameters; and v_{i0} denotes the random intercept for patient i for $i = 1, 2, \ldots, 27$ and $j = 0, 1, 2, 3$. This model is fitted to the data in **aspart.ss3** as described below.

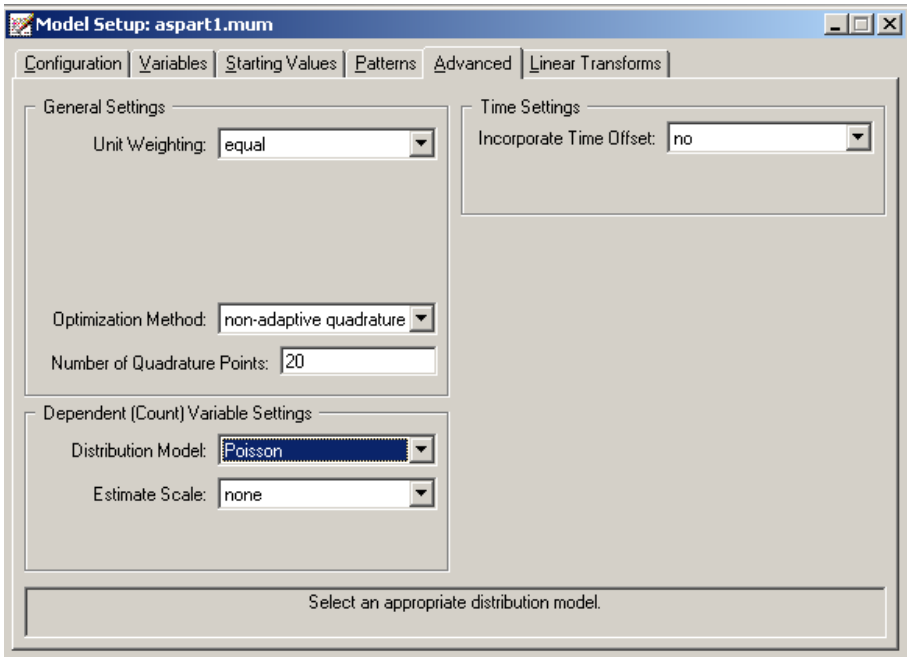
3.1.2.2 Setting up the analysis

Start by opening the SuperMix spreadsheet **aspart.ss3**. Select the **New Model Setup** option on the **File** menu to load the **Model Setup** window. On the **Configuration** tab, enter the titles 2 level Poisson log random intercept model and ASPART data for the analysis in the **Title 1** and **Title 2** text boxes respectively. The count outcome variable Headache is selected from the **Dependent Variable** drop-down list box. The **Dependent Variable Type** drop-down list box is used to indicate that the outcome variable is a count. The variable ID, which defines the levels of the hierarchy, is selected as the **Level-2 ID** from the **Level-2 IDs** drop-down list box.



Next, click on the **Variables** tab to proceed with variable selection. The variables Period1, Period2, Period3, Period4, and DrugAsp are specified as the fixed effects of the model by checking the **E** check boxes for Period1, Period2, Period3, Period4, and DrugAsp in the **Available** grid. These actions produce the following **Variables** tab. By default, an intercept model is included in the fixed part of the model, along with a random intercept at level 2.





Finally, we click on the **Advanced** screen and keep all the default settings as shown above, except for those concering the method of estimation. Select **non-adaptive quadrature**, and set the quadrature points to 20. Before we can run the analysis, we have to save the model specifications to a file. This is accomplished by using the **Save** option on the **File** menu to open a **Save Mixed Up Model** dialog box. First enter the name **aspart1.mum** in the **File name**

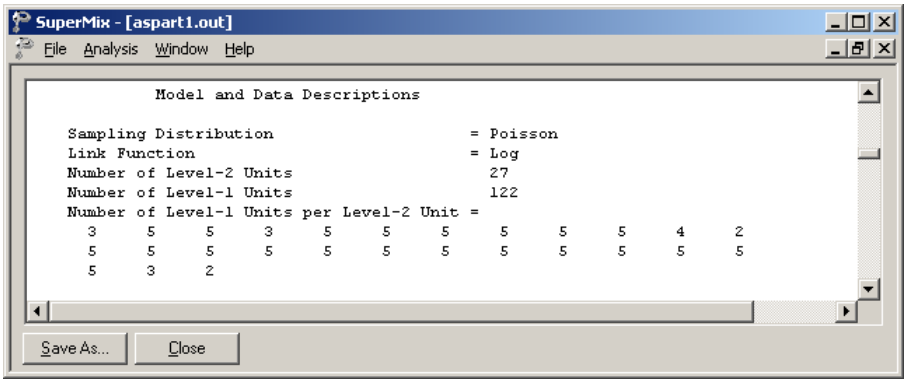
text box and then click on the **Save** button to save the file. The analysis is run by selecting the **Run** option from the **Analysis** menu. This produces the corresponding output file **aspart1.out**.

3.1.2.3 Discussion of results

Portions of this output file are shown below.

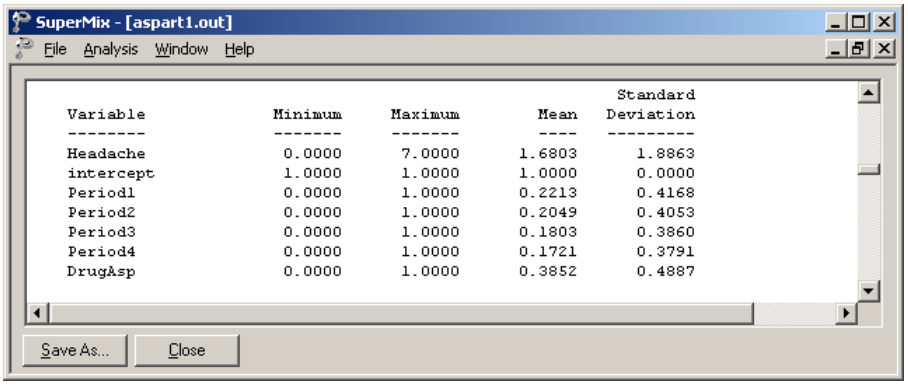
Model and data description

The output file indicates that there are 27 subjects with 122 observations nested within them. The number of observations per subject varies between 2 and 5.



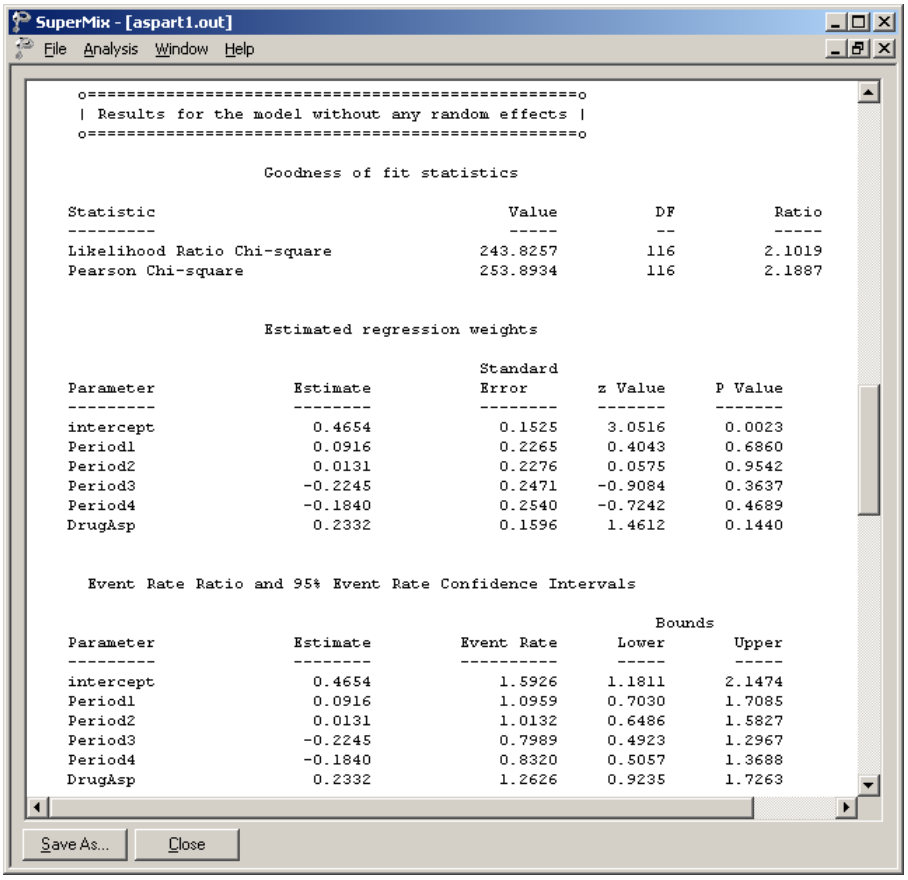
Descriptive statistics

The descriptive statistics for all the variables is shown next. The variance of Headache is $1.8863^2 = 3.5581$, which is substantially larger than the mean 1.6803. This might conflict with our assumption that the Poisson distribution is an appropriate choice for these data. This can be verified by fitting a negative binomial model with a small dispersion parameter.



Results for the model without any random effects

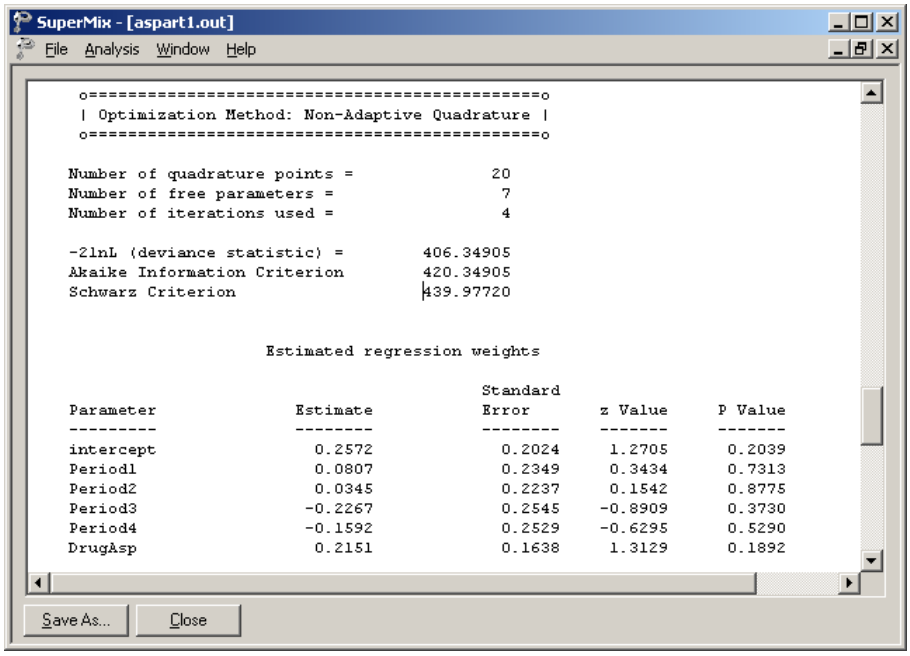
The results for the model without any random effects are shown below. In this section the goodness of fit statistics, estimated regression weights and event rate ratio and 95% event rate confidence intervals are included.



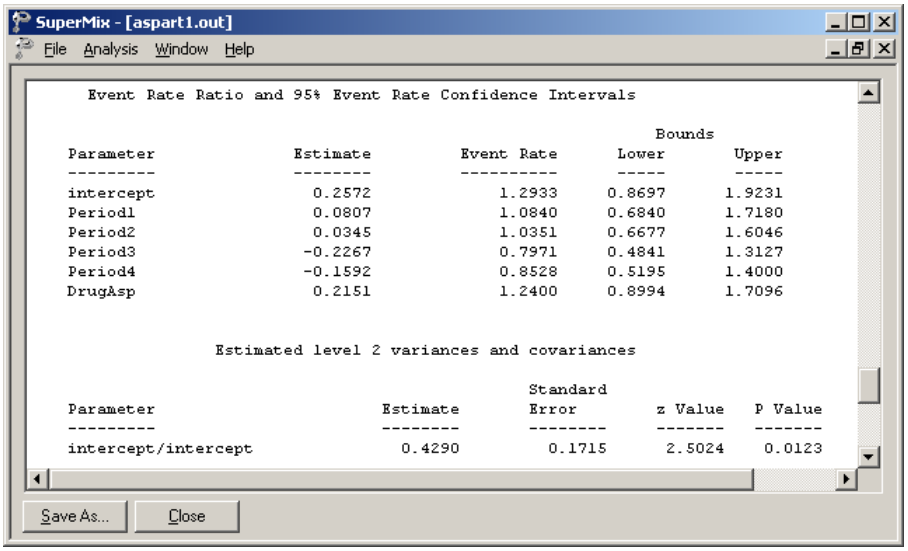
Fixed and random effect results

The final results are shown next. The number of iterations needed for convergence and the deviance information are given first, followed by the estimates.

The random-effect standard deviation is estimated as .643, and although a Wald test rejects the hypothesis that this parameter equals 0, use of the Wald test for testing whether variance parameters equal zero is questionable, since the Wald test is based on the assumption that parameters can assume any real value. Regarding the regression coefficients, all effects are non-significant. The results indicate that the model does not fit the data very well.



The event ratio and 95% event rate confidence interval and estimated level-2 variances and covariances are shown next to the estimated regression weights. The event ratios are the exponents ($e^{\hat{\beta}}$) of the estimated regression coefficients.



The random-effect variance is estimated as 0.429, and although a Wald test rejects the hypothesis that this parameter equals 0, use of the Wald test for testing whether variance parameters equal zero is questionable, since the Wald test is based on the assumption that parameters can assume any real value. Regarding the regression coefficients, all effects are non-significant. The results indicate that the model does not fit the data very well.

3.1.2.4 Interpreting the results

Estimated outcomes for groups: unit-specific results

The expected number of headaches can be obtained in the following fashion. First, we substitute the estimated coefficients in the model formulation

$$\begin{aligned}\log\left(\hat{\text{Headache}}_{ij}\right) &= \hat{\beta}_0 + \hat{\beta}_1 \times \text{Period1}_{ij} + \hat{\beta}_2 \times \text{Period2}_{ij} \\ &\quad + \hat{\beta}_3 \times \text{Period3}_{ij} + \hat{\beta}_4 \times \text{Period4}_{ij} + \hat{\beta}_5 \times \text{DrugAsp}_{ij} \\ &= 0.2572 + 0.0807 \times \text{Period1}_{ij} + 0.0345 \times \text{Period2}_{ij} \\ &\quad -0.2267 \times \text{Period3}_{ij} - 0.1592 \times \text{Period4}_{ij} + 0.2151 \times \text{DrugAsp}_{ij}.\end{aligned}$$

or, after taking exponents on both sides, as

$$\begin{aligned}\hat{\text{Headache}}_{ij} &= \exp(0.2572 + 0.0807 \times \text{Period1}_{ij} + 0.0345 \times \text{Period2}_{ij} \\ &\quad -0.2267 \times \text{Period3}_{ij} - 0.1592 \times \text{Period4}_{ij} + 0.2151 \times \text{DrugAsp}_{ij}).\end{aligned}$$

As an example, we calculate the expected number of headaches for a typical patient to whom aspartame was administered (DrugAsp = 1). During the first treatment period, we find that for such a patient

$$\begin{aligned}\hat{\text{Headache}}_{ij} &= \exp(0.2572 + 0.0807 + 0.2151) \\ &= 1.7385.\end{aligned}$$

The expected numbers of headaches for a typical patient (again with DrugAsp = 1) for the second, third, and fourth treatment periods are calculated as

$$\begin{aligned}\hat{\text{Headache}}_{ij} &= \exp(0.2572 + 0.0345 + 0.2151) \\ &= 1.6600,\end{aligned}$$

$$\begin{aligned}\hat{\text{Headache}}_{ij} &= \exp(0.2572 - 0.2267 + 0.2151) \\ &= 1.2784,\end{aligned}$$

and

$$\begin{aligned}\hat{\text{Headache}}_{ij} &= \exp(0.2752 - 0.1592 + 0.2151) \\ &= 1.3677\end{aligned}$$

respectively. Complete results for all groups are given in Table 5.2.

Estimated outcomes for groups: population-average results

The latent response variable model,

$$y_{ij} = \mathbf{z}'_{(1)ij}\mathbf{b}_i + \mathbf{x}'_{(1)ij}\boldsymbol{\beta}_{(1)} + e_{ij},$$

makes the assumption that e_{ij} : $LID(0, \sigma_e^2)$. For a Poisson distribution it is assumed that $\sigma_e^2 = 1$. Under the assumption that $\mathbf{v}_i$ and e_{ij} are independently distributed, it follows that

$$\sigma^2_{y_{ij}} = \mathbf{z}'_{ij}\boldsymbol{\Phi}_{v_i}\mathbf{z}_{ij} + \sigma_e^2.$$

The design effect d_{ij} is defined as

$$d_{ij} = \frac{\sigma^2_{y_{ij}}}{\sigma_e^2},$$

which, for the current model, may be calculated as

$$d_{ij} = \frac{\sigma^2_{y_{ij}}}{\sigma_e^2} = \frac{\text{var}\left(v_{i0}\right) + 1}{1} = 1.4290$$

where $\text{var}\left(v_{i0}\right) = 0.4290$, with v_{i0} denoting the random intercept coefficient. The estimated population-average probabilities (Hedeker & Gibbons, 2006) are obtained in a similar fashion as the unit-specific probabilities, after replacing the exponent in the formula used for calculation of the estimated unit-specific probabilities with $\text{exp} = \text{exp}/\sqrt{d_{ij}}$ as shown below.

$$\begin{aligned}\widehat{\text{Headache}}_{ij} = \text{exp}[&(0.2572 + 0.0807 \times \text{Period1}_{ij} + 0.0345 \times \text{Period2}_{ij} - 0.2267 \times \text{Period3}_{ij} \\ &-0.1592 \times \text{Period4}_{ij} + 0.2151 \times \text{DrugAsp}_{ij}) / \sqrt{1.4290}].\end{aligned}$$

The expected unit-specific and population average probabilities are summarized in Table 5.3. We see that there is very little difference in the estimated number of headaches. This result is to be expected as the design effect is $\sqrt{1.4290} = 1.1954$.

Table 5.3: Estimated unit-specific and population average results for groups

DRUGASP	Period	Estimated headaches (unit-specific)	Estimated headaches (population-average)
0	1	1.4020	1.1728
0	2	1.3387	1.1199
0	3	1.0310	0.8624
0	4	1.1030	0.9227
1	1	1.7385	1.4543
1	2	1.6600	1.3886
1	3	1.2784	1.0694
1	4	1.3677	1.1441