arkov

day of length

3	4	5
7.6	7.3	7.1
7.1	7.1	7.0
10.7	10.4	10.2
6.9	6.8	6.5
6.8	6.6	6.4
10.9	10.4	10.0

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g the i-th case

$\hat{\boldsymbol{\theta}})(\boldsymbol{\theta} - \hat{\boldsymbol{\theta}})$

ollows

$\frac{\boldsymbol{\theta})}{\theta_n}|_{\boldsymbol{\theta}=\hat{\boldsymbol{\theta}}}$

pproximation is

the summation

Table 3.4: model prediction type 2 - First order Markov

Nb days used	1-step Dev.	Joint Dev.	Taking Compliance	Drug holiday of length 1	2	3	4	5
Random intercept model								
31	2530	2675	0.08	7.4	7.8	8.0	7.6	7.3
21	2614	2775	0.08	7.8	7.3	7.4	7.3	7.2
11	2678	2853	0.10	9.2	8.6	8.8	8.7	8.6
Random parameters model								
31	2596	2713	0.08	7.2	7.0	7.1	6.8	6.5
21	2710	2880	0.09	8.3	6.9	6.7	6.4	6.2
11	2776	2957	0.11	9.9	8.5	8.3	8.1	8.0

$$\frac{\partial^2 l_{(i)}(\boldsymbol{\theta})}{\partial\theta_m \partial\theta_n} = \sum_{(i)} [\frac{1}{h(y_i \mid \boldsymbol{\theta})} \frac{\partial^2 h(y_i \mid \boldsymbol{\theta})}{\partial\theta_m \partial\theta_n} - \frac{1}{h^2(y_i \mid \boldsymbol{\theta})} \frac{\partial h(y_i \mid \boldsymbol{\theta})}{\partial\theta_m} \frac{\partial h(y_i \mid \boldsymbol{\theta})}{\partial\theta_n}]$$

Denoting $\eta_{iqk} = X_{ik}\boldsymbol{\beta} + \gamma B_q$, with B_q from the Gauss-Hermite approximation, the derivatives of the individual marginal likelihood can be approximated for the logit link as

$$\left[\begin{array}{l} \frac{\partial h(y_i|\boldsymbol{\theta})}{\partial\theta_m} = \sum_{q=1}^{Q}\sum_{k=1}^{n_i} \frac{y_{ik}+(y_{ik}-1)e^{\eta_{iqk}}}{1+e^{\eta_{iqk}}} \frac{\partial\eta_{iqk}}{\partial\theta_m} g(y_i \mid \boldsymbol{\theta}, B_q) A(B_q) \\ \frac{\partial^2 h(y_i|\boldsymbol{\theta})}{\partial\theta_m\partial\theta_n} = \sum_{q=1}^{Q}\sum_{k=1}^{n_i} [\frac{y_{ik}+(y_{ik}-1)e^{\eta_{iqk}}}{1+e^{\eta_{iqk}}} \frac{\partial\eta_{iqk}}{\partial\theta_m} \frac{\partial g(y_i|\boldsymbol{\theta},B_q)}{\partial\theta_n} - \\ \qquad \frac{e^{\eta_{iqk}}}{(1+e^{\eta_{iqk}})^2} \frac{\partial\eta_{iqk}}{\partial\theta_n} \frac{\partial\eta_{iqk}}{\partial\theta_m} g(y_i \mid \boldsymbol{\theta}, B_q)] A(B_q) \end{array}\right.$$

If $\hat{\boldsymbol{\theta}}_{(i)}$ is not too different from $\hat{\boldsymbol{\theta}}$ and $l_{(i)}(\boldsymbol{\theta})$ is locally quadratic, the one-step estimator should be close to the fully iterated value (Cook and Weisberg 1995). Applied to our data, its computation time was just 1 percent of the original time and corresponding results are presented in table 3.4.

As with observed compliance data, we find it useful to plot the cumulative predicted number of doses taken over time against time (days). In figures 3.4, each plot represents for a given patient the observed compliance (full line) and simulated predictions (dotted lines). The model used for prediction is the type 1, first order Markov random parameters model estimated on 31 days. We conclude that the model predicts compliance well.