Modeling Longitudinal Count Data with Excess Zeros and Time-Dependent Covariates: Application to Drug Use

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Presentation Outline

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VI Example Data Analysis: EMA
EMA Example and Data Issues
Motivating Example

EMA: Ecological Momentary Assessment

- Interest: Honest Reporting of Marijuana Usage
- Connection to Craving, Motivation, Social Context
Motivating Example

EMA: Ecological Momentary Assessment

- Interest: Honest Reporting of Marijuana Usage
- Connection to Craving, Motivation, Social Context
- Subjects recruited based on usage history, physiological testing
- Respond to text messages 3 times per day for 14 consecutive days.
Properties of the Data

EMA Data:

- Count Response Variable
- Longitudinal Responses
- Excess Zeros Expected (And Observed)
- Predictors Change Over Time
Correlated Count Regression Models
Ordinary Count Regression Models

Poisson regression:

Random Component: Poisson Distribution

\[ Y_i \sim \text{Poi}(\lambda(x_i)) \]

Systematic and Link Components: Log Link

\[ \ln(\lambda(x_i)) = x_i^T \beta \]
Ordinary Count Regression Models

Parameter Estimation typically proceeds using Maximum Likelihood (implemented using Iterative Re-Weighted Least Squares)

\[ l(\beta; y, x) = \sum_{i=1}^{N} [y_i \ln(\lambda(\beta; x_i)) - \lambda(\beta; x_i) - \ln(y_i!)] \]

Hypothesis Testing performed using Wald Statistics

Implicitly assumes \( \text{Var}(Y_i) = \mathbb{E}[Y_i] \)
Overdispersion

When $\text{Var}(Y_i) > \mathbb{E}[Y_i]$ the data are overdispersed

Positive autocorrelation in the data leads to overdispersion

Consequence: Inflation of Type I Error Rate
Correlated Count Regression Models

Accounting for autocorrelation in count responses:

**Conditional Models:** Include random subjects effects
Subject-Specific Interpretations
Correlated Count Regression Models

Accounting for autocorrelation in count responses:

Conditional Models: Include random subjects effects
   Subject-Specific Interpretations

Marginal Models: Determine marginal moments directly
   Population-Averaged Interpretations
Conditional Correlated Count Regression

Mixed Poisson Count Regression:

Random Component: Poisson Distribution / Gamma Random Effect

\[ Y_{it} | u_i \sim \text{Poi}(\lambda(x_{it}, z_{it})) \]
\[ u_i \sim \text{Gamma}(\alpha, \beta) \]

Systematic and Link Components: Log Link, Random Effects Design

\[ \ln(\lambda(x_{it}, z_{it})) = x_{it}^T \beta + z_{it}^T v(u) \]
Conditional Correlated Count Regression

Parameter Estimation:

Maximum Likelihood, h-Likelihood, Markov Chain Monte Carlo, EM Algorithm

The above model is often referred to as a Random Intercept model. Sometimes Random Slopes models are applied, adding columns from $X$ to $Z$. 
Marginal Correlated Count Regression

Marginal Correlated Poisson Count Regression:

Random Component: Mean and Variance Specified

\[ Y_{it} \sim \mathcal{D} \left( \lambda(x_{it}), \phi V(\lambda(x_{it})) \right) \]

The marginal model is specified through the mean and variance structure, as defining a quasi-likelihood.
The mean is specified through the link and systematic components:

$$\ln(\lambda(x_{it})) = x_{it}^T \beta$$

The variance-covariance structure is specified directly:

$$V(\lambda(x_{it})) = A_i^{1/2} R_i(\alpha) A_i^{1/2}$$
Marginal Correlated Count Regression

Estimate parameters by solving estimating equations:

\[
\sum_{i=1}^{N} \left( \frac{\partial \lambda(\beta; x_i)}{\partial \beta} \right)^T [\phi V_i(\lambda(\beta; x_i))]^{-1} (Y_i - \lambda(\beta; x_i)) = 0
\]

- Dispersion parameters estimated similarly, using GEE2
- Test hypotheses using Sandwich Wald Tests / Generalized Score Tests
Time-Dependent Covariate Estimation
Time-Dependent Covariates

Predictors that include variation both between and within subjects

- Exogenous versus Endogenous
- External versus Internal
- Also “Time-Varying Covariates” or “Within-Subjects Covariates”
Consider three approaches:

1. **Conditional Models**: Mixed Correlated Count Regression
2. **Marginal Models**: GEE for Count Regression
3. **Marginal Models**: GMM for Count Regression
Conditional Time-Dependent Covariate Models

Directly split coefficients into “within” and “between” components (Neuhaus and Kalbfleisch (1998)).

Traditional Mixed Poisson:

\[
\ln(\lambda(x_{it}, z_{it})) = \beta_0 + \beta_1 x_{it} + z_{it}^T v(u)
\]
Conditional Time-Dependent Covariate Models

Directly split coefficients into “within” and “between” components (Neuhaus and Kalbfleisch (1998)).

Traditional Mixed Poisson:

\[
\ln(\lambda(x_{it}, z_{it})) = \beta_0 + \beta_1 x_{it} + z_{it}^T v(u)
\]

Mixed Poisson with TDC Decomposition:

\[
\ln(\lambda(x_{it}, z_{it})) = \beta_0 + \beta_1 B \bar{x}_i + \beta_1 W (x_{it} - \bar{x}_i) + z_{it}^T v(u)
\]
Coefficient interpretations:

$\beta_B$ represents the expected effect on the (transformed) response mean from changes across individuals

$\beta_W$ represents the expected effect on the (transformed) response mean from changes within individuals
Marginal Time-Dependent Covariate Models: GEE

GEE Approach: For longitudinal data, Pepe and Anderson (1994) argued

- Use a **diagonal working correlation** structure
  
or

- Verify the sufficient condition:

  \[ E[Y_{it}|X_{it}] = E[Y_{it}|X_{ij}, j = 1, \ldots, T] \]

Either will guarantee the expectation of the GEE is the **zero vector**
Marginal Time-Dependent Covariate Models: GEE

GEE Approach:

- Use of “Independent” working correlation structure recommended
- Fitzmaurice (1995) noted losses in efficiency with this approach
- Efficiency depends on strength of autocorrelation
Marginal Time-Dependent Covariate Models: GMM

Generalized Method of Moments Approach:

- Lai and Small (2007) proposed a method of avoiding diagonal working correlation structures

- Idea: Select combinations of derivative and residual terms **without** a working correlation structure

- Ensure that expectation is zero, depending on nature of time-dependent covariate
Marginal Time-Dependent Covariate Models

GMM Process: Minimum Quadratic Form estimation

Minimize

\[ Q(\beta) = G^T(\beta; Y, X)W^{-1}G(\beta; Y, X) \]

Where \( G(\beta; Y, X) \) is an average vector of valid moment conditions constructed according to the type of TDC such that

\[ E[G(\beta; Y, X)] = 0 \]
Models for Correlated Counts with Excess Zeros
Excess-Zero Count Model Options

Hurdle Poisson:
- “Certain Zero” comes from one process
- Once “hurdle” is cleared, responses are positive

Zero-Inflated Poisson:
- “Zero” comes from two processes
- Either “Certain Zero” or part of Poisson process
Excess-Zero Correlated Count Model Options

Correlated Count Model Options:

1. **Conditional Models**: Mixed Hurdle
2. **Conditional Models**: Mixed ZIP
3. **Marginal Models**: Hurdle GEE
Conditional Model: Mixed Hurdle Poisson Model

Mixed Hurdle Poisson Distributional Component

\[ Y_{ij} | u_i \sim \text{HurP}(\pi(x_{it}, z_{it}; u_i), \lambda(x_{it}, z_{it}; u_i)) \]

\[ u_i \sim \mathcal{N}(0, \sigma^2_u) \]

\[ f_{ij}(y_{ij} | u_i; \pi_{it}, \lambda_{it}) = \begin{cases} 
\pi_{it} & y_{ij} = 0 \\
(1 - \pi_{it}) \frac{f(y_{ij} | u_i; \lambda_{it})}{1 - f(0; \lambda_{it})} & y_{ij} > 0 
\end{cases} \]
Conditional Model: Mixed ZIP Model

Mixed Zero-Inflated Poisson Distributional Component

\[ Y_{ij} | u_i \sim ZIP(\pi(x_{it}, z_{it}; u_i), \lambda(x_{it}, z_{it}; u_i)) \]

\[ u_i \sim \mathcal{N}(0, \sigma^2_u) \]

\[ f_{ij}(y_{ij} | u_i; \pi_{it}, \lambda_{it}) = \begin{cases} 
\pi_{it} + (1 - \pi_{it})f(0; \lambda_{it}) & y_{ij} = 0 \\
(1 - \pi_{it})f(y_{ij} | u_i; \lambda_{it}) & y_{ij} > 0 
\end{cases} \]
Conditional Model: Mixed ZIP Model

Mixed Hurdle / ZIP Systematic Components

\[
\logit(\pi_{it}) = x_{l, it}\alpha + z_{it}u \\
\ln(\lambda_{it}) = x_{c, it}\beta + z_{it}u
\]
Conditional Modeling

Mixed Hurdle and ZIP Models:

- Estimation proceeds using likelihood methods (MCMC)
- Time-dependent covariates can again be split into “within” and “between” effects
- Models show high Type I Error rates in the presence of time-dependent covariates
Marginal Modeling: Hurdle GEE

GEE for “zero-inflation” presented by Dobbie and Welsch (2001)

Construct two response vectors:

- Binary: “Certain Zero” Indicator:
  \[ Y_{bin,it} \sim \mathcal{D}(\pi_{it}, \pi_{it}(1 - \pi_{it})) \]

- Count: “Positive” counts with Positive Poisson Moments:
  \[ Y_{it}|(y_{it} > 0) \sim \mathcal{D}(\mu(\lambda_{it}), V(\lambda_{it})) \]
Marginal Modeling: Hurdle GEE

Hurdle GEE: Construct two models:

- Binary Response:
  \[
  \text{logit} (\pi(z_{it})) = z_{it}^T \alpha
  \]

- Positive Count Response:
  \[
  \ln (\lambda(x_{it})) = x_{it}^T \beta
  \]
Marginal Modeling: Hurdle GEE

Hurdle GEE: Solve two estimating equations:

\[
\sum_{i=1}^{N} \left( \frac{\partial \pi_i}{\partial \alpha} \right) V_{l,i}^{-1} (y_{bin} - \pi_i) = 0
\]

\[
\sum_{i=1}^{N} \left( \frac{\partial \mu_i}{\partial \beta} \right) V_{c,i}^{-1} (I(y_i > 0)) (y_i - \mu_i) = 0
\]

(Use Independent Working Correlation Structure for Time-Dependent Covariates)
Hurdle Generalized Method of Moments
Why not use existing methods?

- Need to account for autocorrelation, excess zeros, time-dependent covariates
- Other methods have a **single treatment for all Time-Dependent Covariates**
- Marginal method (Independent GEE) imposes independence assumption, with consequences of lost efficiency
Hurdle GMM: Model

Joint Quasi-Generalized Linear Model: Random Components

- Certain Zero:
  \[ Y_{bin,it} = I(Y_{it} = 0) \sim \mathcal{D}(\pi_{it}, \pi_{it}(1 - \pi_{it})) \]

- Positive Count:
  \[ Y_{it} | (y_{it} > 0) \sim \mathcal{D}(\mu(\lambda_{it}), V(\lambda_{it})) \]
Hurdle GMM: Model

Joint Quasi-Generalized Linear Model: Random Components

- Positive Count:
  \[
  \mu(\lambda_{it}) = \frac{\lambda_{it}}{1 - e^{-\lambda_{it}}}
  \]

- Variance:
  \[
  V(\lambda_{it}) = \mu(\lambda_{it}) [1 - \lambda_{it} + \mu(\lambda_{it})]
  \]
Joint Quasi-Generalized Linear Model: Systematic Components

- Certain Zero:
  \[ \logit (\pi(z_{it})) = z_{it}^T \alpha \]

- Positive Count:
  \[ \ln (\lambda(x_{it})) = x_{it}^T \beta \]
Hurdle GMM: General Process

Hurdle GMM Process: Independently Minimize Quadratic Forms:

\[
Q_l(\alpha) = (G_l(\alpha; Y, Z))^T W_l^{-1} (G_l(\alpha; Y, Z))
\]

\[
Q_c(\beta) = (G_c(\beta; Y, X))^T W_c^{-1} (G_c(\beta; Y, X))
\]
Hurdle GMM: General Process

Hurdle GMM Process: Select **Valid** Moment Conditions:

\[
G_l(\alpha; Y, Z) = \frac{1}{N} \sum_{i=1}^{N} g_{l,i}(\alpha; Y_i, Z_i)
\]

\[
G_c(\beta; Y, X) = \frac{1}{N} \sum_{i=1}^{N} g_{c,i}(\beta; Y_i, X_i)
\]

\[
E[g_{l,ij}] = E[g_{c,ij}] = 0
\]
Hurdle GMM: General Process

Hurdle GMM Process: Structure of Valid Moment Conditions:

\[ g_{l,ij}(\alpha; Y_i, Z_i) = \frac{\partial \pi(z_{is})}{\partial \alpha_k} \left( I(Y_{it}=0) - \pi(z_{it}) \right) \]

\[ g_{c,ij}(\beta; Y_i, X_i) = \frac{\partial \mu(\lambda(x_{is}))}{\partial \beta_k} \left( I(Y_{it}>0)[Y_{it} - \mu(\lambda(x_{is}))] \right) \]

It remains to determine how to construct these Valid Moment Conditions
Determining Valid Moment Conditions:

1. “Types” as selected by researcher

2. “Extended Classification” using data
Validity of Moment Conditions depends on the expectation:

$$E_{\beta} \left[ \frac{\partial \mu_{is}}{\partial \beta_j} (Y_{it} - \mu_{it}) \right] = 0$$

Lai and Small (2007) proposed using expected characteristics of individual Time-Dependent Covariates to make decisions on combinations of $s$ and $t$ that would lead to independent components.
Hurdle GMM: Types

- **Type I TDC**: Expectation holds for all $s$ and $t$
- **Type II TDC**: Expectation holds for $s \geq t$
- **Type III TDC**: Expectation holds for $s = t$
- **Type IV TDC**: Expectation holds for $s \leq t$
Hurdle GMM: Types

- **Type I TDC**: The response and time-dependent covariate are associated only at the **same time**.

- **Type II TDC**: The response is associated with **prior values** of the time-dependent covariate.

- **Type III TDC**: A **feedback loop** exists between the time-dependent covariate and the response.

- **Type IV TDC**: The time-dependent covariate is associated with **prior values** of the response.
Hurdle GMM: Types

Construct subject vectors of Valid Moment Conditions using values of $s$ and $t$ that satisfy the chosen “type” of TDC:

$$g_{l,ij}(\alpha; Y_i, Z_i) = \frac{\partial \pi(z_is)}{\partial \alpha_k} (I(Y_{it}=0) - \pi(z_{it}))$$

$$g_{c,ij}(\beta; Y_i, X_i) = \frac{\partial \mu(\lambda(x_is))}{\partial \beta_k} (I(Y_{it}>0)[Y_{it} - \mu(\lambda(x_{it}))])$$
Hurdle GMM: Extended Classification

Extended Classification Process:

1. Estimate derivative, residual terms of expectation using initial estimates (Independent GEE)

2. Select Valid Moment Conditions *individually* based on empirical independence of standardized derivative, residual terms (using all subjects)

3. Construct vectors of Valid Moment Conditions using empirically supported combinations of $s$ and $t$
Hurdle GMM: Extended Classification

Using initial parameter estimates, calculate component-wise independent vectors:

\[
\hat{d}_{sj} = \frac{\partial \hat{\mu}_s}{\partial \beta_j}
\]

\[
\hat{r}_t = y_t - \hat{\mu}_t
\]

Standardized Values:

\[
\tilde{d}_{sji} \text{ and } \tilde{r}_{ti}
\]
Hurdle GMM: Extended Classification

Calculate Correlation:

\[ \hat{\rho}_{sjt} = \frac{\sum (\tilde{d}_{sji} - \tilde{d}_{sj})(\tilde{r}_{ti} - \tilde{r}_t)}{\sqrt{\sum (\tilde{d}_{sji} - \tilde{d}_{sj})^2 \sum (\tilde{r}_{ti} - \tilde{r}_t)^2}} \]

Assuming all fourth moments exist and are finite,

\[ \rho^*_{sjt} = \frac{\hat{\rho}_{sjt}}{\sqrt{\hat{\mu}_{22}/N}} \sim \mathcal{N}(0, 1) \]

\( \hat{\mu}_{22} = (1/N) \sum_i (\tilde{d}_{sji})^2 (\tilde{r}_{ti})^2 \)

Omit potential moment conditions with **significant** association
Hurdle GMM: Estimation Process

0 (Based on Hurdle GEE (Independent), evaluate associations in potential moment conditions)

1 Construct separate vectors of Valid Moment Conditions for two components of Joint Quasi-GLM

2 Using initial parameter estimates, estimate optimal weight matrices for each component

3 Separately minimize two Quadratic Forms for two components of Joint Quasi-GLM
Hurdle GMM: Estimation Options

Implementation of GMM:

- **Two-Step GMM**: Estimate weight matrix $\hat{W}$ using initial parameter estimates, minimize $Q(\beta)$

- **Iterated GMM**: Iterate between estimation of $\hat{W}$ and minimization of $Q(\beta)$

- **Continuously Updating GMM**: Minimize $Q(\beta)$, where $W(\beta)$ is a function of unknown parameters
Hurdle GMM: Two-Step Estimation

Implementation of GMM:

- **Two-Step GMM**: Estimate weight matrix $\hat{W}$ using initial parameter estimates, minimize $Q(\beta)$
- **Iterated GMM**: Iterate between estimation of $\hat{W}$ and minimization of $Q(\beta)$
- **Continuously Updating GMM**: Minimize $Q(\beta)$, where $W(\beta)$ is a function of unknown parameters
Hurdle GMM: Two-Step Estimation

\[ \hat{\alpha} = \arg \min \left[ Q_l(\alpha) \right], \quad \hat{\beta} = \arg \min \left[ Q_c(\beta) \right] \]

\[
\operatorname{Cov}(\hat{\alpha}) = \left( \frac{1}{N} \sum_{i=1}^{N} \frac{\partial g_l}{\partial \alpha} \right)^T \hat{V}_{g_l}^{-1} \left( \frac{1}{N} \sum_{i=1}^{N} \frac{\partial g_l}{\partial \alpha} \right)
\]

\[
\operatorname{Cov}(\hat{\beta}) = \left( \frac{1}{N} \sum_{i=1}^{N} \frac{\partial g_c}{\partial \beta} \right)^T \hat{V}_{g_c}^{-1} \left( \frac{1}{N} \sum_{i=1}^{N} \frac{\partial g_c}{\partial \beta} \right)
\]
Example Data Analysis: EMA
EMA Data Analysis

Predict next usage using craving, controls (day of the week, academics)
Usage over Time

Usage by Study Day

Day of Study

Next Usage

2 4 6 8 10 12 14
0 2 4 6 8 10 12

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Longitudinal Count Data: Excess Zeros and TDC
Usage Reports

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<th>Times Used</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tbody>
<tr>
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<td>318</td>
<td>120</td>
<td>55</td>
<td>25</td>
<td>13</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

48.58% Zeros
Usage and Craving

Next Usage versus Craving

Craving
Next Usage

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Usage and Craving

Usage and Craving by Study Day

Day of Study

Usage and Craving by Study Day

Next Usage / Craving

2 4 6 8 10

0 10
Models Fit

Three models fit:

1. Mixed Hurdle Poisson, with Between / Within Decomposition of “craving”

2. GEE Hurdle, with Independent Working Correlation Structure

3. GMM Hurdle, with “craving” as Type II TDC, Day as Type I TDC
## Model Results

<table>
<thead>
<tr>
<th></th>
<th>Mixed Hurdle</th>
<th>Hurdle IGEE</th>
<th>Hurdle GMM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Logistic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>craving</td>
<td>0.223*** (W)</td>
<td>−0.170***</td>
<td>−0.169***</td>
</tr>
<tr>
<td></td>
<td>−0.219. (B)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>controls</td>
<td>Not Significant</td>
<td>.</td>
<td>**</td>
</tr>
<tr>
<td><strong>Count</strong></td>
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<td></td>
</tr>
<tr>
<td>craving</td>
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<td>0.049**</td>
<td>0.048***</td>
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<tr>
<td></td>
<td>0.160 (B)</td>
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</tr>
<tr>
<td>cum GPA</td>
<td>0.056</td>
<td>−0.056</td>
<td>−0.056***</td>
</tr>
<tr>
<td>controls</td>
<td>Not Significant</td>
<td>.</td>
<td>**</td>
</tr>
</tbody>
</table>
Model Results

- Populations with higher craving:
  - Lower probability of certain zero
  - Higher expected positive count, once hurdle is cleared

- Higher within-subject variation:
  - Higher probability of certain zero
  - Lower expected positive count, once hurdle is cleared
Concluding Remarks

- GMM: Initial Values, Estimation Method
- Simulating “Types” of TDC’s
- GMM Fit Statistics
- ARE versus IGEE
Modeling Longitudinal Count Data with Excess Zeros and Time-Dependent Covariates: Application to Drug Use

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