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Research Article

Bayesian Method of Moments for Modelling Repeated Sedation Measurements

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ABSTRACT
Generalized Methods of Moments approach is very popular among econometricians but is hardly used at all outside of economics, where the slightly more general term estimating equations is preferred. In this study, we prefer using GMM and Bayesian GMM approaches in a medical application. Our aim is to show that the use of generalized methods of moments with an without a Bayesian approach can be a valuable tool in medical applications when response values are clearly correlated and independent variables include categorical data as well as continuous variables.

Keywords: GEE, GMM, Bayesian, WinBUGS, Sedation.

1. INTRODUCTION

Magnetic resonance imaging (MRI) and computerized tomography (CT) require the patient to lie still for periods of up to 60 min. These two diagnostic procedures also require strict immobility and sedation for a successful result. If a child can not remain adequately still for examination, sedation may be necessary. Optimal sedation management of children before MRI and CT has received attention in the last decade [1, 2]. The sedation medications must be chosen carefully for children's safety and effectiveness. Many researches related to the comparison of different sedation medications have been performed successfully [3, 4]. In these studies, for each medication group sedation level were obtained at different time points within the time up to 60 min. In addition to sedation level measurements, the other multiple assessment of the same patient were recorded and the within subject, such as sedation levels at different time point for a given patient, were correlated. This case is an example when a longitudinal study is made with responses being measured repeatedly on the same patient across time.

The Generalized Estimating Equation (GEE) approach introduced by Liang [5], which was developed to extend the Generalized Linear Models (GLM) introduced by Nelder [6], facilitates analysis of data collected in longitudinal and repeated measures designs. GEE use GLM to estimate more efficient and unbiased regression parameters relative to ordinary least squares regression in part because they permit specification of a working correlation matrix that accounts for the form of within-subject correlation of responses on dependent variables of many different distributions, including normal, binomial, and poisson [7].

The generalized method of moments (GMM) is a very general statistical method for obtaining estimates of parameters of statistical models. It is a generalization of the method of moments. GMM estimation was formalized by Hansen [8], and since has become one of the most widely used methods of estimation for models in economics and finance. Unlike maximum likelihood estimation (MLE), GMM does not require complete knowledge of the distribution of the data. Only specified moments derived from an underlying model are needed for GMM estimation.

The theory and notation for GMM presented herein follows the excellent treatment given by Hayashi [9]. Other good textbook treatments of GMM at an intermediate level are given by other authors [10, 11]. The most comprehensive textbook treatment of GMM is the one written by Hall [12]. Lai [13] proposed a GMM marginal regression to analyze longitudinal data, and showed its advantages over the GEE.

In contrast to the classical approach, Bayesian estimation requires the specification of likelihood functions or the data generating mechanism. Because of this reason, Bayesian approach has not been applied to the moment problem for a long time. However, recent developments [14-18] proposed Bayesian method of moment's approach that enables direct Bayesian inference in the method of moment's framework.

Yin [19] proposed the Bayesian generalized method of moments (GMM), which is particularly useful when likelihood based methods are difficult. By deriving the moments and concatenating them together, he builds up a weighted quadratic objective function in the GMM framework.

GMM is hardly used at all outside of economics. However, this study prefers using GMM and Bayesian GMM approaches in a medical application. Cengiz [20] focus on modeling repeated sedation measurements, obtained during magnetic resonance imaging (MRI) and computerized tomography (CT) for children, using GEE. In this study we firstly, focus on the modeling the same repeated sedation measurements using GMM instead of GEE. Secondly, in order to have a Bayesian GMM approach as in Bayesian Analysis [19]. We apply the Markov chain Monte Carlo procedure to sample from the posterior distribution in WinBUGS [21], which has become the standard software for Bayesian analysis. Lastly, we compare the performances of the models used with using AIC, BIC and DIC.

2. MATERIAL AND METHODS

In generalized linear models, the response is assumed to possess a probability distribution of the exponential form. That is, the probability density of the response Y for continuous response variables, or the probability function for discrete responses, can be expressed as

$$f(y/Z_i) = \exp\left\{\frac{y_i\theta_i - b(\theta_i)}{a_i(\phi)} + c(y_i,\phi)\right\} \quad (2.1)$$

For the ith subject ($i = 1,\ldots, n$), we observe yi as the outcome of interest and Z_i as the corresponding covariate vector. Functions a, b, and c determine the specific distribution. The linear predictor $\eta_i = \beta^T Z_i$ can be linked with μ_i ($\mu_i = E(y_i / Z_i)$). The quasi-likelihood estimator can be obtained by solving the score-type equation

$$\sum_{i=1}^{n} D_i v_i^{-1}(y_i - \mu_i) = 0 \quad (2.2)$$

Where, $D_i = \partial\mu_i/\partial\beta$.

In the GMM framework, we define

$u_i(\beta) = D_i v_i^{-1}(y_i - \mu_i)$, $i = 1,\ldots,n$ with the population moment condition

$E\{u_i(\beta)\} = 0$ and the corresponding sample moment condition

$U_n(\beta) = \frac{1}{n}\sum_{i=1}^{n} u_i(\beta)$.

The GMM estimator $(\hat{\beta})$ is obtained by minimizing the following quadratic objective function is as follow

$$Q_n(\beta) = U_n^T(\beta)\sum_n^{-1}(\beta)U_n(\beta). \quad (2.3)$$

where

$$\sum_n(\beta) = \frac{1}{n^2}\sum_{i=1}^{n} u_i(\beta)\, u_i^T(\beta) - \frac{1}{n}U_n(\beta)U_n^T(\beta).$$

In general $(\hat{\beta})$ is computed via a two-stage iterative procedure [19].

The objective function $Q_n(\beta)$ follows a chi-squared distribution when evaluated at β_0 or $\bar{\beta}$. Therefore, we can construct a pseudo-likelihood function $\tilde{L}(y/\beta)$ to replace the original likelihood function $L(y/\beta)$ which may be difficult to derive, where

$$\tilde{L}(y/\beta) \propto \exp\left\{-\frac{1}{2}Q_n(\beta)\right\} = \exp\left\{-\frac{1}{2}U_n^T(\beta)\sum_n^{-1}(\beta)U_n(\beta)\right\}. \quad (2.4)$$

As in the usual MCMC procedure, we can derive the posterior distribution based on $\tilde{L}(y/\beta)$. Given the prior distribution $\pi(\beta)$, the posterior distribution of β is

$$\tilde{\pi}(\beta / y) \propto \tilde{L}(y / \beta)\,\pi(\beta). \quad (2.5)$$

3. RESULTS AND DISCUSSION

Magnetic resonance imaging (MRI) and Computerized tomography (CT) require the patient to lie still for periods of up to 60 minutes. These two diagnostic procedures also require strict immobility and sedation for a successful result. If a child cannot remain adequately still for examination, sedation may be necessary. Optimal sedation management of children before MRI and CT has received attention in the last decade. The sedation medications must be chosen carefully for children's safety and effectiveness.

Cengiz [20] studied effects of four different drugs (Midazolam, Diazepam, Luminal and Cardiac Cocktail) on sedation level of 127 children who received MRI and CT. Group M (n=30) received Midazolam, Group D (n=31) received Diazepam, Group L (n=32) received Luminal and Group C (n=34) received Cardiac Cocktail. Sedation levels were maintained in the range of Ramsey Scale from 1-5 for each 15 min. Systolic Blood pressures, Pulse rates, the number of breathe, oxygen saturation were monitored. The other measurements, which may affect the sedation level, such as weight, disease status, test status, complication status, age and adaptation status, were also recorded.

The mean response (sedation level) was modeled as a multinomial regression model using the explanatory variables such as Systolic Blood pressures, Pulse rates, the number of breathe, oxygen saturation, weight, disease status, test status, complication status, age and adaptation status. The descriptions of predictor values used in the analysis were given in more detail in [20]. They used only GEE approach for modeling.

We first apply GMM approach to the same data and compare the results of parameter estimations obtained [20] with the results we have with using the GMM approach. Table 1 shows the results of GEE and GMM approaches for comparison.

Secondly, for Bayesian approach, we investigated model efficacy in Bayesian Generalized Methods of Moments using MCMC and used WINBUGS to generate chains of length 5000 after a burn-in of 5000, resulting in posterior samples of size 10000. Also we used diffuse priors distributions N (0, 10^8) for all parameters to be estimated. Results of Bayesian GMM approach were given in Table 2.

For model comparison, AIC, BIC for GEE, GMM and Bayesian GMM and Deviance Information Criteria (DIC) for only Bayesian GMM were calculated for all models. The results are shown in Table 3.

Table 1: Comparing the results of GEE and GMM approaches

Parameter	GEE			GMM		
	Estimation	Standard Error	p	Estimation	Standard Error	p
group_c	-4.6158	7.7932	0.5537	-4.5233	15.6919	0.6686
group_d	**-63.0109**	**13.6951**	**<.0001**	**-63.1235**	**27.2959**	**0.0210**
group_l	18.2469	18.4159	0.3218	18.7654	29.3089	0.5336
age	0.0460	0.0980	0.6388	0.0646	0.1701	0.7738
sex	-0.2133	0.2549	0.6388	-0.3234	0.3722	0.5665
disease	-0.2162	0.2474	0.4026	-0.2654	0.3295	0.5117
Weight	-0.0385	0.0228	0.0914	-0.0367	0.0425	0.0646
Comp	0.0641	0.0471	0.1735	0.0741	0.0871	0.4619
test	0.1734	0.1177	0.1408	0.1841	0.2505	0.4888
Adopt	**0.5265**	**0.0811**	**<.0001**	**0.5265**	**0.1265**	**<.0001**
SBP	-0.0052	0.0080	0.5155	-0.0121	0.0133	0.6962
PUL	-0.0076	0.0051	0.1343	-0.0013	0.0089	0.3967
OSAT	-0.0411	0.0769	0.5933	-0.0521	0.1373	0.7649
NB	0.0204	0.0117	0.0821	0.0306	0.0219	0.3524

Table 2: Results of Bayesian GMM Approach

	BAYESIAN GMM							
	node	sd	MC error	%2.5	median	%97.5	start	sample
group_c	-3.1581	6.8734	0.0453	-6.5123	-3.5233	4.1234	1	10000
group_d	**-54.6309**	**2.3451**	**0.0012**	**-56.1235**	**-53.1235**	**-50.1252**	**1**	**10000**
group_l	17.2569	15.341	0.0354	-15.7657	18.7654	23.8754	1	10000
age	0.0160	0.3421	0.0012	-0.1701	0.0146	0.1675	1	10000
sex	-0.3245	0.6534	0.0019	-0.6345	-0.3345	1.7654	1	10000
disease	-0.2346	0.3498	0.0054	-0.83454	-0.23454	1.5643	1	10000
weight	**-0.1234**	**0.0198**	**0.0009**	**-0.6214**	**-0.1254**	**-0.0104**	**1**	**10000**
comp	0.0985	0.1871	0.0129	-0.1087	0.0877	0.2431	1	10000
test	0.1432	0.2875	0.0543	-0.2456	0.1456	0.2346	1	10000
adopt	**0.4631**	**0.1089**	**0.0043**	**0.3459**	**0.5456**	**0.8461**	**1**	**10000**
SBP	-0.0175	0.0194	0.0004	-0.1023	-0.0234	0.2340	1	10000
PUL	-0.0123	0.0112	0.0031	-0.1145	-0.0145	0.0857	1	10000
OSAT	-0.1041	0.2134	0.0123	-0.1098	-0.0987	1.0048	1	10000
NB	0.0120	0.1876	0.0065	-0.0576	0.0456	0.1098	1	10000

Table 3: Comparing of the results of GEE, GMM and Bayesian GMM approaches

		APPROACHES		
		GEE	GMM	BAYESIAN GMM
CRITERIA	AIC	34.123	34.289	**29.854**
	BIC	31.765	31.815	**29.975**
	DIC	-	-	**26.154**

4. CONCLUSION

We compared the parameter estimation from the GMM approach with the ones from the GEE approach in Table 1. It is easy to say there is no distinguishes for main effects between both methods and the parameter estimates are identical for all parameters in both methods. We can say that the GMM approach yields asymptotically the same result as the GEE approach for our medical application.

In Table 2, the results of Bayesian GMM approach were given. Table 2 shows group_d, weight and adopt parameters are significant predictor of sedation level, whereas only group_d and adopt parameters are significant predictor of sedation level for both GEE and GMM approaches.

We also calculated AIC, BIC for GEE and GMM and AIC, BIC and DIC for Bayesian GMM for comparisons. The results in Table 3 show that Bayesian GM approach gives the smaller values than GEE and GMM whereas GEE and GMM give the similar AIC and BIC values.

The use of generalized methods of moments can be a valuable tool in medical applications when response values are clearly correlated and independent variables include categorical data as well as continuous variables. Furthermore it can be said that Bayesian GMM improves the model accuracy for this medical application.

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