**A Robust Procedure for GEE Model**

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**Abstract**

In longitudinal studies, multiple measurements are taken on the same subject at different points in time. Thus, observations for the same subject are correlated. This paper proposes a robust procedure for estimating parameters of regression model when generalized estimating equation (GEE) applied to longitudinal data that contains outliers. The procedure is a combination of the iteratively reweighted least square (IRLS) and least trimmed square (LTS) methods and is called *iteratively reweighted least trimmed square* (IRLTS). We conducted a simulation study for gamma model and Poisson model using the proposed method, the result shows that our approach can provide a better result than the classical GEE.

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**Keywords**: longitudinal data, outlier, regression model.

# 1 Introduction

In [statistics](https://en.wikipedia.org/wiki/Statistics), generalized estimating equation (GEE) is used to [estimate](https://en.wikipedia.org/wiki/Estimator) the parameters of a [generalized linear model](https://en.wikipedia.org/wiki/Generalized_linear_model) (GLM) with a possible unknown [correlation](https://en.wikipedia.org/wiki/Correlation_and_dependence) between outcomes. It is a general statistical approach to fit a marginal model for longitudinal data analysis, and it has been popularly applied into clinical trials and biomedical studies. GEEs belong to a class of regression techniques that are referred to as [semiparametric](https://en.wikipedia.org/wiki/Semiparametric_model) because they rely on specification of only the first two [moments](https://en.wikipedia.org/wiki/Moment_%28mathematics%29). Under correct model specification and mild regularity conditions, parameter estimates from GEEs are [consistent](https://en.wikipedia.org/wiki/Consistency_%28statistics%29). The generalized estimating equation approach requires correct specification of the first two moments of a model. However, these moment assumptions can be distorted by contaminated or irregular measurements namely outliers. As a result, the generalized estimating equation method fails to give consistent estimators, and more seriously this will lead to incorrect conclusions [1][8]. In this situation, we need a robust method that can minimize the effect of outliers.

In recent years a few authors have considered robust methods for longitudinal data analysis, see e.g. Qaqish and Preisser [3], Gill [2], Jung and Ying [4], Wang and Zhu [11] and Abebe et al. [1]. In this paper, we combine the IRLS and LTS for obtaining a robust estimation of GEE when data contain outliers. We have shown the effectiveness of this procedure for normal model [7]. In this paper we apply the proposed procedure to gamma and Poisson models.

**2 Generalized Estimating Equation**

Let the vector of measurements on the *i*th subject be **Y***i* = [*Yi*1, ... ,*Yi ni*]T with corresponding vector of means **µ**i = [*µi*1, ... ,*µi ni*]T and **X***i* = [X*i*1, ... ,X*i ni*]T be the *ni*x*p* matrix of covariates. In general, the components of **Y***i*, are correlated but **Y***i* and **Y***k* are independent for any *i ≠* *k*. To model the relation between the response and covariates, we can use a regression model similar to the generalized linear models:

*g*(**µ***i*) = ***η****i* = **X***i* **β**

where **µ***i*= E(**Y**i|**X**i), *g* is a specified link function, and **β** = [*β1, ... ,βp*]T is a vector of unknown regression coefficients to be estimated. The GEE of Liang and Zeger [5] for estimating the *p*×1 vector of regression parameters **β** is is given by :



where **V*i*** be the covariance matrix of **Y***i* modeled as ***V***i=, **A***i* is a diagonal matrix of variance functions *v*(µ*ij*), and **R**(**α**) is the working correlation matrix of **Y***i* indexed by a vector of parameters **α**. Solutions to Eq. (2) are obtained by alternating between estimation of λ, **α** and θ. There are several specific choices of the form of working correlation matrix **R***i*(**α**) commonly used to model the correlation matrix of **Y***i*, among them are *exchangeable* and *autoregressive* correlation matrices.

Solving for **β** is done with iteratively reweighted least squares (IRLS). The following is an algorithm for fitting the specified model using GEEs as described by Johnson and Stokes [3] and Qaqish and Preisser [8]:

1. Compute an initial estimate of , for example with an ordinary generalized linear model assuming independence.
2. A current estimate  is updated by regressing the working response vector on **X**. A new estimate  is obtained by :

 (1)

where  is a block diagonal weight matrix whose ith block is the *ni*x*ni* matrix .

1. Use  to update , where 
2. Iterate until convergence.

**3 Iterated Reweighted Least Trimmed Square**

Let us briefly recall that the robust estimation of regression parameters using LTS [9] method is given by:



where  are the ordered squared residuals, from smallest to largest. LTS is calculated by minimizing the *h* ordered squares residuals, where *h* can be chosen between the range , with *n* being sample size and number of parameters, respectively. One can refer to e.g. [9][10] for some details on LTS method.

The IRLTS procedure is stated in the following short algorithm. To motivate this method, it is convenient to write the algorithm with involving the residuals.

1. Compute an initial estimate of  using IRLS, use the estimate to calculate fitted value : 
2. Calculate residuals : . Sort  for *i* = 1,2,…, *t* and *j* = 1,2,…, *n* in ascending order : 
3. Choose *h* observations which have the lowest *h*-residuals, we denote as subset H
4. Improve estimates of **β** by solving  based on subset H using IRLS
5. Iterate until convergence.
6. **Simulation Study**

We compare the performances of IRLTS and IRLS through simulation study. Two types of outcomes are considered, continuous and count responses. The models for data generation are as follows:

1/µij = β0+β1 x1ij + β2 x2ij

Log (µij) = β0+β1 x1ij + β2 x2ij

where βks for k=0,1,2 are randomly generated, i=1,2,… 200 and j=1,2,..,5..The covariates x1ij are i.i.d. from a uniform distribution Unif(1,5), and x2 is the measurement time variable, i.e. x2i = 1,2,3,4,5. For each scenario, we generate the data based on the underlying true correlation structures as exchangeable (EXCH) with 𝛼=0.5. For the first model (inverse link) the gamma distributed model is used, and for the second model (log link) the Poisson distributed model is applied. In this simulation, 1000 Monte Carlo data sets are generated for each scenario. We considered contamination proportion in data ε= 5%, 10%, 20% and 30%. We evaluate the results using the mean square error (MSE) of the parameter estimates.

We provide the expected values and MSEs of parameter estimates resulted from our simulation on Table 1- Table 4. Table 1 and Table 2 show the expected values and MSEs of parameter estimates for the first model, while Table 3 and Table 4 for the second model.

Table 1. The expected values, standard errors and MSEs of for gamma distributed model with exchangeable correlation matrix

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Method** | **Classical GEE** | | | **IRLTS** | | |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 1.833421 | 0.417356 | 0.419098 | 1.292539 | 0.280084 | 0.080563 |
| 10% | 1.963008 | 0.551804 | 0.694453 | 1.343505 | 0.345998 | 0.119739 |
| 20% | 2.105067 | 0.522999 | 0.861099 | 1.302799 | 0.245013 | 0.061308 |
| 30% | 2.158723 | 0.712847 | 1.180859 | 1.432421 | 0.581205 | 0.346613 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.664892 | 0.297197 | 0.205406 | 0.957103 | 0.034595 | 0.003693 |
| 10% | 0.587415 | 0.348410 | 0.297492 | 0.968876 | 0.075239 | 0.007119 |
| 20% | 0.314225 | 0.347369 | 0.600688 | 0.964959 | 0.039372 | 0.003323 |
| 30% | 0.297561 | 0.338291 | 0.617832 | 0.937923 | 0.088894 | 0.012682 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.743453 | 0.289166 | 0.174850 | 0.974127 | 0.039936 | 0.006689 |
| 10% | 0.549449 | 0.423348 | 0.425292 | 0.958451 | 0.018566 | 0.007922 |
| 20% | 0.355655 | 0.349199 | 0.597828 | 0.975630 | 0.032734 | 0.005954 |
| 30% | 0.332191 | 0.336312 | 0.621917 | 0.969043 | 0.071512 | 0.010960 |

Table 2. The expected values, standard errors and MSEs of for gamma distributed model with autoregressive correlation matrix

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Method** | **Classical GEE** | | | **IRLTS** | | |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 1.713422 | 0.174403 | 0.127509 | 1.169724 | 0.219998 | 0.102270 |
| 10% | 2.051958 | 0.292341 | 0.476604 | 1.172668 | 0.169948 | 0.081395 |
| 20% | 2.096749 | 0.279746 | 0.561178 | 1.182726 | 0.281815 | 0.127424 |
| 30% | 2.208355 | 0.570003 | 0.975395 | 1.094088 | 0.105856 | 0.105908 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.746269 | 0.169773 | 0.087549 | 0.977105 | 0.032371 | 0.001180 |
| 10% | 0.493787 | 0.257591 | 0.311197 | 0.974237 | 0.026179 | 0.000892 |
| 20% | 0.290721 | 0.257720 | 0.553459 | 0.982542 | 0.035247 | 0.001279 |
| 30% | 0.228004 | 0.231963 | 0.595925 | 0.981851 | 0.023087 | 0.000579 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.739142 | 0.224797 | 0.132593 | 0.981539 | 0.021532 | 0.002405 |
| 10% | 0.511909 | 0.302973 | 0.355672 | 0.981291 | 0.028264 | 0.002762 |
| 20% | 0.281145 | 0.270400 | 0.627330 | 0.983924 | 0.028529 | 0.002551 |
| 30% | 0.225163 | 0.377600 | 0.646722 | 1.003760 | 0.035796 | 0.001758 |

As shown in Table 1 and Table 2, our approach (IRLTS) performs better than the classical GEE. The MSEs of IRLTS are smaller than the MSEs of classical GEE, the outliers influence the estimation of ,  and . The parameter estimates of classical GEE are much more influenced than the parameter estimates of IRLTS. The more outliers contained in the data the larger the deviation of classical GEE estimates from the parameter value. In Table 3 and Table 4, the behavior of MSEs of both methods is the same as the first case, here we can see that IRLTS performs better than the classical GEE because the MSEs of IRLTS are smaller than the MSEs of classical GEE.

Table 3. The expected values, standard errors and MSEs of  for Poisson distributed model with exchangeable correlation matrix

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Method** | **Classical GEE** | | | **IRLTS** | | |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 7.851928 | 0.578389 | 49.012922 | 2.242959 | 0.411831 | 1.041084 |
| 10% | 9.299508 | 0.776268 | 71.575965 | 2.084935 | 0.454712 | 1.670854 |
| 20% | 10.710302 | 0.425014 | 96.915019 | 2.351178 | 0.546663 | 1.478125 |
| 30% | 11.413164 | 0.621123 | 111.439999 | 1.988002 | 0.486656 | 1.475743 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.309635 | 0.108437 | 0.418891 | 1.052717 | 0.059291 | 0.014543 |
| 10% | 0.194983 | 0.044670 | 0.568586 | 1.011790 | 0.074132 | 0.009602 |
| 20% | 0.097441 | 0.077894 | 0.729016 | 0.918343 | 0.038557 | 0.002349 |
| 30% | 0.092040 | 0.031461 | 0.733153 | 0.809874 | 0.101063 | 0.029211 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.281547 | 0.064601 | 0.478304 | 0.947537 | 0.021808 | 0.000986 |
| 10% | 0.159566 | 0.060507 | 0.660655 | 0.967633 | 0.065401 | 0.004284 |
| 20% | 0.087528 | 0.031481 | 0.779957 | 0.900333 | 0.028748 | 0.005696 |
| 30% | 0.067109 | 0.035320 | 0.816673 | 0.825752 | 0.057643 | 0.024164 |

The result for Poisson model shows similar behavior to the result for gamma model. For the result of Poisson model in Table 3 and Table 4, IRLTS also performs better than the classical GEE. The MSEs of IRLTS are smaller than the MSEs of classical GEE, the outliers influence the estimation of ,  and . The parameter estimates of classical GEE are much more influenced than the parameter estimates of IRLTS. The more outliers contained in the data the larger the deviation of classical GEE estimates from the parameter value. In Table 3 and Table 4, the behavior of MSEs of both methods is the same as the first case, here we can see that IRLTS performs better than the classical GEE.

The estimation of IRLTS yields better results than classical GEE for both case we considered here. The MSEs of IRLTS is smaller than classical GEE, this means that IRLTS can reduce the influence of the high leverage points better than the classical GEE.

Table 4. The expected values, standard errors and MSEs of  for Poisson distributed model with autoregressive correlation matrix

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Method** | **Classical GEE** | | | **IRLTS** | | |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 8.493574 | 0.689463 | 40.055071 | 1.614313 | 0.331758 | 0.455831 |
| 10% | 9.788645 | 0.962589 | 58.478701 | 1.765065 | 0.204619 | 0.523307 |
| 20% | 10.525858 | 0.877176 | 70.050502 | 2.356166 | 0.470975 | 0.724548 |
| 30% | 10.635832 | 0.570803 | 71.449706 | 3.071576 | 0.974599 | 1.054251 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.309635 | 0.108437 | 0.418891 | 1.052717 | 0.059291 | 0.014543 |
| 10% | 0.194983 | 0.044670 | 0.568586 | 1.011790 | 0.074132 | 0.009602 |
| 20% | 0.097441 | 0.077894 | 0.729016 | 0.918343 | 0.038557 | 0.002349 |
| 30% | 0.092040 | 0.031461 | 0.733153 | 0.809874 | 0.101063 | 0.029211 |
|  |  |  |  |  |  |  |
| ε |  |  | MSE |  |  | MSE |
| 5% | 0.281547 | 0.064601 | 0.478304 | 0.947537 | 0.021808 | 0.000986 |
| 10% | 0.159566 | 0.060507 | 0.660655 | 0.967633 | 0.065401 | 0.004284 |
| 20% | 0.087528 | 0.031481 | 0.779957 | 0.900333 | 0.028748 | 0.005696 |
| 30% | 0.067109 | 0.035320 | 0.816673 | 0.825752 | 0.057643 | 0.024164 |

**5 Concluding Remark**

In this paper we have shown that our proposed procedure can minimize the effect of outliers on parameter estimation; IRLTS can produce a relatively efficient and consistent estimator compared to the classical GEE (IRLS). Base on the MSE, IRLTS performs much better than the classical GEE for gamma and Poisson models.

**References**

1. A. Abebe, J. W. McKean, J. D. Kloke and Y. Bilgic, Iterated Reweighted Rank-Based Estimates for GEE Models, Technical Report. (2014).
2. P. S. Gill, A Robust Mixed Linear Model Analysis for Longitudinal Data*. Statistics in Medicine*, **19** (2000), 975-987.
3. G. Johnston and M. Stokes, Repeated Measures Analysis With Discrete Data Using The SAS System. *SUGI Proceeding*. SAS Institute Inc., Cary, NC, (1996).
4. S. H. Jung and Z. Ying, Rank-Based Regression With Repeated Measurements Data, Biometrika, **90** (2003), 732-740.
5. K. Y. Liang and S. L. Zeger, Longitudinal Data Analysis Using Generalized Linear Models. *Biometrika*, **73** (1986), 13-22.
6. P. McCullagh and J. A. Nelder, *Generalized Linear Models*, Chapmann and Hall, London, 1989.
7. K. Nisa and N. Herawati. 2017. Robust Estimation of Generalized Estimating Equation when Data Contain Outliers. *INSIST*. In Press.
8. B. F. Qaqish and J. S. Preisser, Resistant fits for regression with correlated outcomes an estimating equations approach. *Journal of Statistical Planning and Inference*, **75** (1999), 15-431.
9. R. J. Rousseeuw and A. M. Leroy, *Robust Regression and Outlier Detection*, Wiley, New York, 1987.
10. P. J. Rousseeuw and K. van Driessen, Computing LTS Regression for Large Data Sets. *Data mining and Knowledge Discovery*, **12** (2006), 29-45.
11. Y. G. Wang and M. Zhu, Rank-based regression for analysis of repeated measures. *Biometrika*, **93** (2006), 459-464.