Media Statistika

p-ISSN 1979 – 3693 e-ISSN 2477 – 0647
MEDIA STATISTIKA 16(2) 2023: 124-135
http://ejournal.undip.ac.id/index.php/media_statistika

PERFORMANCE OF NEURAL NETWORK IN PREDICTING MENTAL HEALTH STATUS OF PATIENTS WITH PULMONARY TUBERCULOSIS: A LONGITUDINAL STUDY

Lalu Ramzy Rahmanda[1], Adji Achmad Rinaldo Fernandes[1], Solimun[1], Lucius Ramifidisoa[2], Armando Jacquis Federal Zamelina[1]
[1] Department of Statistics, Brawijaya University, Indonesia
[2] Department of Mathematical Informatics, University of Antsiranana, Madagascar

e-mail: *ramzyrahmanda@student.ub.ac.id*

DOI: 10.14710/medstat.16.2.124-135

Article Info:
Received: 27 November 2023
Accepted: 27 January 2024
Available Online: 26 February 2024

Keywords:
Artificial Neural Network, GLMM, Mental Health, Longitudinal Data Analysis, Pulmonary Tuberculosis

Abstract: Comorbidity between pulmonary tuberculosis and mental health status requires effective psychiatric treatment. This study aims to predict anxiety and depression levels in patients with pulmonary tuberculosis and consider future mental health treatment for patients. A sample of 60 pulmonary tuberculosis patients in Malang were involved and evaluated longitudinally every two weeks over 13 periods. In this study, we use the Generalized Neural Network Mixed Model (GNMM) to obtain better results in predicting anxiety and depression levels in patients with pulmonary tuberculosis and compare the results with the Generalized Linear Mixed Model (GLMM). The flexibility of GLMM in modeling longitudinal data, and the power of neural network in performing a prediction makes GNMM a powerful tool for predicting longitudinal data. The result shows that neural network's prediction performance is better than the classical GLMM with a smaller MSPE and fairly accurate prediction. The MSPEs of the three compared models: 1-Layer GNMM, 2-Layer, and GLMM, respectively are 0.0067, 0.0075, 0.0321 for the anxiety levels, and 0.0071, 0.0002, and 0.0775 for the depression levels. Furthermore, future research needs to investigate the data with a larger sample size or high dimensional data with large network architectures to prove the robustness of GNMM.

1. INTRODUCTION

Tuberculosis (TB) contributes considerably to the human disease burden and remains one of the world's deadliest infectious diseases. World Health Organization (WHO) (2022) reported that tuberculosis disease in Indonesia had the second highest TB burden globally, after India. The number of tuberculosis cases in Indonesia is estimated at 969 thousand cases. This is increasing from cases in 2020 with 824 thousand cases. Of the estimated tuberculosis cases reported in Indonesia, 92% were confirmed to be pulmonary tuberculosis. However, controlling pulmonary tuberculosis relies heavily on accurate diagnosis, appropriate treatment, effective monitoring, and evaluation of treatment.

Mental health is a significant factor that complicates treatment outcomes for people with infectious diseases like tuberculosis, and chronic diseases such as HIV/AIDS and

cancer. Previous research has examined the impact of mental health on tuberculosis patients, identifying anxiety and depression as major mental health problems associated with the tuberculosis disease. Anxiety, as described by Gumantan et al. (2020), is a mental health disorder marked by intense feelings of worry, distress, or fear that can impede daily functions and ultimately weaken the immune system. Moynihan et al. (2022) also stated that anxiety can result from disappointment, discontent, and insecurity. Notably, anxiety is separate from fear. Depression is a mental illness defined by symptoms such as diminished interest or pleasure, decreased energy, feelings of guilt or low self-worth, sleep and appetite disturbances, tiredness, and impaired concentration. It can have a chronic or recurrent course and significantly impact an individual's daily activities. In extreme cases, depression can result in suicide (Suryani et al., 2016). Depression is a severe medical disorder that affects behaviour, emotions, and cognition, and requires formal treatment from various sources for improvement, but it is not inherently permanent.

For patients with pulmonary tuberculosis to successfully complete their treatment, they must enrol in the Directly Observed Treatment Short Course (DOTS) program, which is designed to help them adhere to their medication regimen (Rahmi et al., 2017). The Health Research and Development Agency of the Republic of Indonesia has discovered that non-adherence among TB patients is a significant factor in the low rate of cure coverage. The article by Jong highlights the psychosocial impact, which includes emotional issues such as boredom, lack of motivation, and more severe mental disorders, such as depression (Suryani et al., 2016). Screening for depression and anxiety is crucial in identifying patients requiring further psychiatric treatment and support (Wang et al., 2018). Agbeko et al. (2022) found that mental health had a significant impact on tuberculosis outcomes, particularly in relation to anxiety and depression. Similarly, Hayward et al. (2021) reported an increase in tuberculosis incidence among patients with mental illnesses, such as depression and schizophrenia.

Longitudinal studies are critical for enhancing the understanding of the development and persistence of disease in the health sciences. These studies can address fundamental questions by assessing within-individual changes in the response variable through repeated measurements of the same individuals over time (Fitzmaurice et al., 2004). Verbeke and Molenberghs (2000) introduced the Generalized Linear Mixed Model (GLMM) analysis method for longitudinal data. The GLMM model calculates two effects: the initial one being a fixed effect, which analyzes the influence of treatment and concomitant variables. The second effect is random, accounting for individual subject differences (subject-specific).

In recent years, there has been a swift increase in the development of Artificial Neural Networks (ANN), including within the statistical field. ANN are highly effective predictive models that can handle the size and intricacy of big datasets, but they presume that input observations are independent. Because mental health data are frequently collected over time, the use of neural network models that disregard the correlation structure may introduce bias when predicting future health outcomes. Most existing neural network architectures lack the ability to model longitudinal data collected from repeated measurements in the same subject. While a GLMM is powerful in modeling longitudinal data, it falls short in terms of predictive power. On the other hand, ANN are powerful prediction tools, but they assume that input observations are independent. GNMM expands on the conventional feed-forward neural network structure by introducing a random effect element, which improves the accuracy of longitudinal and other correlated data forecasts. The model is organized like a GLMM, the linear fixed effect of which is replaced by a feed-forward neural network. With ANNs' predictive ability and the GLMM's adaptability to handle non-independent data, GNMM has

become a powerful tool for forecasting correlated data.

However, GLMM has limitations as the researcher needs to specify a parametric form for the relationships between all variables. Typically, these relationships are not known before conducting the analysis, making it challenging to capture high nonlinear relationships (Cascarano et al., 2023). In contrast, neural networks are well-suited for modeling complex nonlinear relationships.

2. LITERATURE REVIEW

2.1. Longitudinal Data

Longitudinal data combines cross-sectional and time series data, providing observations from N independent subjects observed repeatedly over T periods. In contrast, cross-sectional studies only collect a single data point from each subject (Diggle et al., 2006; Wu & Zhang, 2006). Thus, the essential distinction between longitudinal and cross-sectional data is that longitudinal data tend to exhibit correlation within a subject and independence between subjects, whereas cross-sectional data generally exhibit independence. The notation for longitudinal data is as follows: Given $i = 1,2, \dots, m$ individuals, each with repeated observations $j = 1,2, \dots, n_i$. The number of repeated observations for individuals does not have to be the same, resulting in $N = \sum_{i=1}^{m} n_i$ total observations the time of observation denoted by t_{ij}, the response variable expressed as $\boldsymbol{Y_{ij}}$, which is a vector of size n_i with the observation value y_{ij}. The explanatory factors are represented as a matrix $\boldsymbol{X_i}$ with the dimension of $n_i \times p$, where p denotes the number of predictors. $\boldsymbol{Y_i} = (\boldsymbol{Y_{i1}}, \dots, \boldsymbol{Y_{in}})^T$ is the vector of repeated measures.

2.2. Generalized Linear Mixed Model (GLMM)

Longitudinal data in practice often lacks balance, leading to the adoption of a two-stage analysis approach. In this method, a linear regression function is fitted specifically for each subject. The two-stage model is described as follows:

(1) Stage 1: In this stage, Y_{it} represents the observed response for the i-th individual/subject at the t-th period, where $i = 1, \dots, N$; and $t = 1, \dots, T$ is presented in Equation (1)

$$\boldsymbol{Y_{it}} = \boldsymbol{Z_{it}\beta_{it}} + \boldsymbol{\varepsilon_{it}} \quad (1)$$

(2) Stage 2: In the second stage, The multivariable regression model used to explain within-subject variability is associated with subject-specific regression coefficients β_i, as presented in Equation (2).

$$\boldsymbol{\beta_i} = \boldsymbol{K_i\beta} + \boldsymbol{b_i} \quad (2)$$

By combining the two-stage analysis into a single statistical model, i.e., by substituting β_i in Equation (2) into Equation (1), a GLMM is obtained. The GLMM obtained from the combination of the two-stage analysis is given by Equation (3) below.

$$\boldsymbol{Y_i} = \boldsymbol{X_i\beta} + \boldsymbol{Z_i b_i} + \boldsymbol{\varepsilon_i} \quad (3)$$

Where $\boldsymbol{X_i} = \boldsymbol{Z_i K_i}$ is a matrix of known independent variables with dimensions $(n_i \times p)$. The model assumes a vector of repeated measurements that follows a linear regression model with a population-specific parameter, β (i.e., the same for all subjects), and a subject-specific parameter, b_i. b_i is considered random and is therefore referred to as a random effect (Verbeke & Molenberghs, 2000).

The assumptions that must be met for GLMM are the assumption of residual normality. GLMM assumes that the random effects b_i $(i = 1,2, \dots m)$ are independent and

identically distributed (Rohmaniah & Chandra, 2018). Several statistical tests have been developed to assess the normality of residuals, including the Anderson-Darling, Shapiro-Wilk, and Kolmogorov-Smirnov tests. To test the normality assumption of residuals using the Shapiro-Wilk test, follow these steps: (Hanusz & TarasiŃska, 2014).

$$\boldsymbol{H_0 : \varepsilon_i} \sim \mathrm{N}(0,\boldsymbol{\sigma^2}) \text{ vs } \mathrm{H}_1 : \varepsilon_i \not\sim \mathrm{N}(0,\boldsymbol{\sigma^2})$$

The Equation (4) presented the test statistic.

$$\boldsymbol{W} = \frac{(\sum_{i=1}^{n} \boldsymbol{a_i X_{i:n}})^2}{\sum_{i=1}^{n} (\boldsymbol{X_i} - \bar{\boldsymbol{X}})^2} \tag{4}$$

Description: $X_{i:n}$ is order statistics $X_{1:n} \leq X_{2:n} \leq \cdots \leq X_{n:n}$ for random sample $X_1, X_2, \ldots, X_n$; $\bar{X}$ is mean of sample.

$$\boldsymbol{a_i}: \boldsymbol{a_1}, \boldsymbol{a_2}, \ldots, \boldsymbol{a_n} = \frac{\boldsymbol{m^T V^{-1}}}{\left(\boldsymbol{m^T V^{-1} V^{-1} m^T}\right)^{1/2}}$$

2.3. Generalized Neural Network Mixed Model (GNMM)

Many prior studies have utilized neural networks for prediction. For instance, Poli and Jones (2012) suggested a neural network approach to prediction using Bayesian inferential procedures for algorithmic derivation with respect to the Newton algorithm. Efron (2020) employed neural networks for prediction, estimation, and attribution, with the study conducted using a small sample size. Finally, Mandel et al. (2021) proposed a novel technique known as the GNMM for analyzing longitudinal and clustered data. The GNMM model shows high potential in accurately predicting outcomes and addressing underlying noise in complex datasets without requiring strong assumptions.

Based on the equation (3), y_{it} are conditionally independent with means $E(y_{it}|b_i) = \mu_{it}^b$ and variances $var(y_{it}|b_i) = \phi a_{it} v(\mu_{it}^b)$, where $v(.)$ is a known variance function, a_{it} is a known constant, and ϕ is a fixed dispersion parameter. In generalized linear models, the mean is related to a linear predictor through a link function. The goal of the GNMM is to modify this formulation for neural networks by substituting the fixed effect part of the linear predictor with the output of a feed-forward neural network.

Consider a feed-forward ANN with L hidden layers, x_{it} as the p inputs, and a single output with μ_{it}^b. The neural network's output μ_{it}^b is a nonlinear function of the predictors x_{it}, with the network weights $\omega^{(l)}$, and biases $\delta^{(l)}$. This is achieved through a series of nested activation functions $g_l(.)$ for each layer l, where $l = 0,1,\ldots,L$. The input enters the neural network through the L -th hidden layer, which consists of nodes that produce:

$$\boldsymbol{\alpha_{it}^{(L)}} = \boldsymbol{g_L}\left(\boldsymbol{\omega^{(L)} x_{it}} + \boldsymbol{\delta^{(L)}}\right) \tag{5}$$

With $\boldsymbol{\omega^{(L)}}$ is a $k_L \times p$ weight matrix; $\boldsymbol{\delta^{(L)}}$ is a bias vector of length k_L; $g_L(.)$ is the input vector undergoes an element-wise application of the activation function $g_l(.)$.

For the l-th hidden layer (l=1,…,L−1) with kl nodes, the layer's output is:

$$\boldsymbol{\alpha_{it}^{(l)}} = \boldsymbol{g_l}\left(\boldsymbol{\omega^{(l)} \alpha_{it}^{(l+1)}} + \boldsymbol{\delta^{(l)}}\right) \tag{6}$$

Where $\boldsymbol{\omega^{(l)}}$ is a $k_l \times k_{(l+1)}$ matrix; $\delta^{(l)}$ is length of k_l

Finally, the univariate neural network output is related to the outcome's conditional mean.

$$\boldsymbol{\mu_{it}^b} = \boldsymbol{g_0}\left(\boldsymbol{\omega^{(0)} \alpha_{it}^{(1)}} + \boldsymbol{\delta^{(0)}} + \boldsymbol{z_{it}^T b_i}\right) \tag{7}$$

where $\boldsymbol{\omega^{(0)}}$ is $1 \times k_1$. This is similar to the classical GLMM framework (Breslow & Clayton, 1993), with the exception that the linear predictor portion for the fixed effects is substituted

with $\omega^{(0)}\alpha_{it}^{(1)} + \delta^{(0)}$, the output of a feed-forward neural network and a non-linear function of a specified variable x_{it} described by Equations (1)-(3). The final activation function $g_0(.)$ serves a similar role to the inverse of the link function in GLMM. Figure 1 illustrates the overall architecture of GNMM.

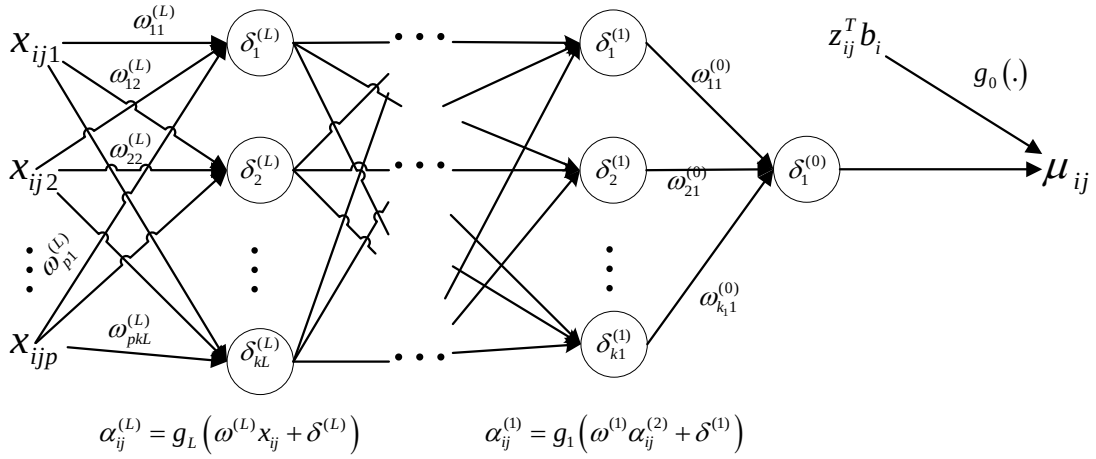


Figure 1. The General Architecture of Generalized Neural Network Mixed Model with Multi-layer Network

The model assumes that $\boldsymbol{b} = (b_1, b_2, \ldots b_m)^T$ follows a multivariate normal distribution with mean $\mathbf{0}$ and covariance $\boldsymbol{D}(\boldsymbol{\theta})$, which may be dependent on an unknown vector of variance components $\boldsymbol{\theta}$. The quasi-likelihood function is utilized to estimate the model parameters as described in Equation (8).

$$|\boldsymbol{D}|^{-1/2} \int \exp\left(\frac{\mathbf{1}}{\boldsymbol{\phi}} \sum_{\boldsymbol{i=1}}^{\boldsymbol{N}} \sum_{\boldsymbol{t=1}}^{\boldsymbol{T}} \int_{\boldsymbol{y_{it}}}^{\boldsymbol{\mu_{it}}^{\boldsymbol{b}}} \frac{\boldsymbol{y_{it}} - \boldsymbol{u}}{\boldsymbol{a_{it}} \boldsymbol{v(u)}} d\boldsymbol{u} - \frac{\mathbf{1}}{\mathbf{2}} \boldsymbol{b}^{\boldsymbol{T}} \boldsymbol{D}^{-\mathbf{1}} \boldsymbol{b} - \boldsymbol{\lambda}(\boldsymbol{\omega}^{\boldsymbol{T}} \boldsymbol{\omega} + \boldsymbol{\delta}^{\boldsymbol{T}} \boldsymbol{\delta}) d\boldsymbol{b}\right) \quad (8)$$

Where $\boldsymbol{\omega}$ represents the combined vectorization of the matrices $\boldsymbol{\omega}^{(\mathbf{0})}, \boldsymbol{\omega}^{(\mathbf{1})}, \ldots \boldsymbol{\omega}^{(\boldsymbol{L})}$ into a single column vector, $\boldsymbol{\delta}$ represents the concatenation of the matrices $\boldsymbol{\delta}^{(\mathbf{0})}, \boldsymbol{\delta}^{(\mathbf{1})}, \ldots, \boldsymbol{\delta}^{(\boldsymbol{L})}$ into a column vector, and λ is the regularization parameter used for a ridge penalty.

We compare the prediction accuracy of GLMM and GNMM using their respective mean square prediction errors (MSPEs), which are provided below.

$$\begin{aligned} MSPE_{\widehat{GNMM}} &= E\left(\boldsymbol{y_{it}} - \boldsymbol{g_0}(\widehat{\boldsymbol{N}}_{\boldsymbol{it}})\right)^2 \\ MSPE_{\widehat{GLMM}} &= E\left(\boldsymbol{y_{it}} - \boldsymbol{g_0}(\widehat{\boldsymbol{M}}_{\boldsymbol{it}})\right)^2 \end{aligned} \quad (9)$$

where, $\widehat{\boldsymbol{N}}_{\boldsymbol{it}} = \hat{\omega}^{(0)}\alpha_{it}^{(1)} + \hat{\delta}^{(0)} + \boldsymbol{z}_{\boldsymbol{it}}^{\boldsymbol{T}}\hat{b}_i$ and $\widehat{\boldsymbol{M}}_{\boldsymbol{it}} = x_{it}^T\hat{\beta} + \boldsymbol{z}_{\boldsymbol{it}}^{\boldsymbol{T}}\hat{b}_i$

3. MATERIAL AND METHOD

3.1. Data and Participants

This study was conducted over 13 periods. The patients' evaluations were executed every 2 weeks during the 6-month treatments (weeks 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24). The data was collected from the Saiful Anwar General Hospital, Malang (2022). This longitudinal study enrolled 60 patients with pulmonary tuberculosis disease, for individuals who met the criteria as follows:

(1) The data is complete and balanced, indicating that patients were routinely monitored throughout the 13 observation periods

(2) Only patients with new cases of pulmonary tuberculosis, not relapse cases, were included in this study
(3) The patient is following anti-tuberculosis drug therapy
(4) Patients aged between 25 – 50 years

3.2. Psychiatric Tools

In this study, the Indonesian version of the Hospital Anxiety and Depression Scale (HADS) was used to determine the levels of anxiety and depression that the patient is experiencing. The Hospital Anxiety and Depression Scale (HADS) developed by Zigmond & Snaith (1983) is a 14-item measure designed to assess anxiety and depression symptoms in medical patients, with an emphasis on reducing the impact of physical illness on the total score. The depression items tend to focus on the anhedonic symptoms of depression. The HADS produces two scales, one for anxiety (HADS–A) and one for depression (HADS–D). The validity and reliability of this questionnaire were tested by Rudy, et al. (2015) and showed that the questionnaire is valid and reliable to use in Indonesia.

3.3. Statistical Tools

To predict anxiety and depression levels in patients with pulmonary tuberculosis, we utilized Mandel et al. (2021) proposed GNMM model. Our implementation involved a 1-layer network with three nodes and a random intercept, along with a 2-layer network featuring three nodes in the first layer and two nodes in the second layer. We compared our results to those obtained from employing the GLMM, which had a main effect and random intercept. Additionally, we calculated the MSPE across all subjects. The data analysis was carried out using R Studio.

4. RESULTS AND DISCUSSION

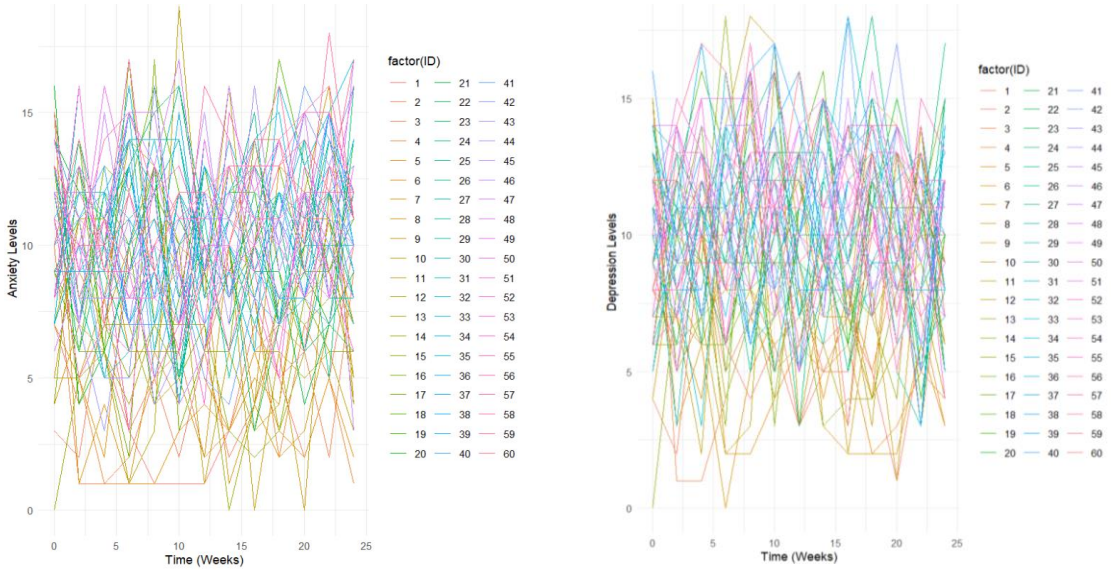
4.1. Trajectories of Anxiety and Depression Levels Over Time

In recent years, there has been an increasing emphasis on the mental well-being of individuals with tuberculosis (TB) due to the identified link between psychiatric disorders, particularly anxiety and depression, and unfavorable treatment results in TB patients. The plot of the mean response trajectory in longitudinal data presents a graphical depiction of how the observed variable progresses and changes over time. This plot enables us to detect patterns, trends, and variations in our dataset, assisting us in answering inquiries such as whether there is a significant surge over time, a drastic modification at a specific juncture, or any unexpected oscillations. Figure 2 depicts the anxiety and depression levels' trajectories over time.

Figures 2(a) and 2(b) show the longitudinal changes in mean response over time, showing the anxiety and depression levels of 60 patients during the 6-months treatment period. The plots shown in Figure 2 are challenging to understand because there is overplotting making it hard to see the individuals. In Figure 3 and Figure 4, we provide the individual plots of anxiety and depression levels of the first 10 patients with pulmonary tuberculosis, as 60 individual plots is too many to comprehend.

Based on Figures 3 and 4, we can monitor and learn the distribution and changes in anxiety and depression levels for each patient during the treatment phase. The mental health status of each patient appears to be different for each patient in the first measurement. In general, the plots for anxiety and depression show similar patterns across time for each individual indicating an interaction between anxiety and depression. Finally, we utilize

GNMM to predict the anxiety and depression levels of patients afflicted with pulmonary tuberculosis.



(a) (b)

Figure 2. The Trajectory of Mean Responses over Time. (a) Trajectory of Anxiety Levels Over Time; (b) Trajectory of Depression Levels Over Time

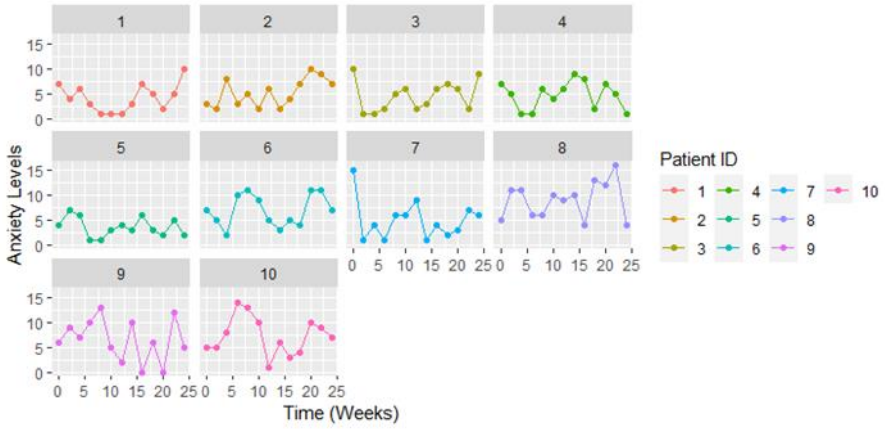


Figure 3. The Trajectory of Anxiety Levels of The First 10 Individuals Over Time

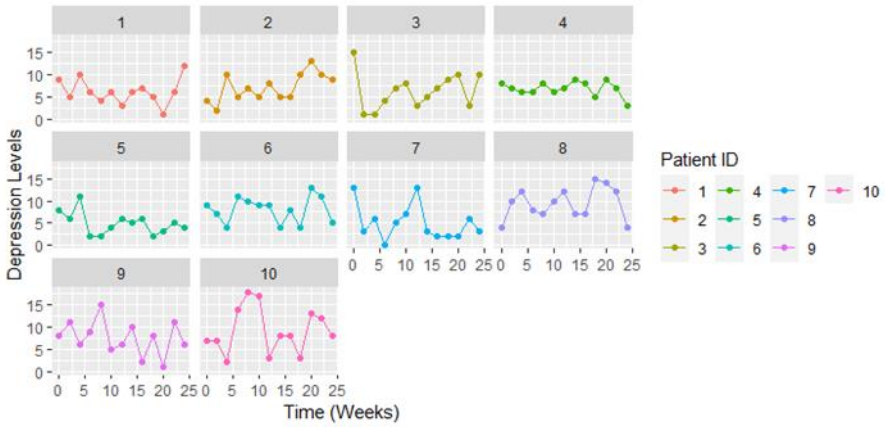


Figure 4. The trajectory of Depression Levels of The First 10 Individuals Over Time

4.2. Mental Health Prediction in Pulmonary Tuberculosis Patients

In this study, the mental health status of 60 patients with pulmonary tuberculosis who met the criteria was measured and collected continuously every two weeks over 6 months. In this study, mental health refers to the anxiety and depression levels of each patient. Lara-Espinosa & Hernández-Pando (2021) reported that there is significant comorbidity between tuberculosis and mental illness, and the treatment of patient with tuberculosis must be made integrally with the treatment of anxiety and depression. This is because anxiety and depression are factors that can influence the compliance and well-being of the patient. The mental health status is measured based on the total score of the HADS questionnaire. A total score of 0-7 shows a normal level of anxiety and depression, a total score of 8-10 indicates that the patient has a borderline case of anxiety and depression, and 11-21 indicates that the patient has a problem with their mental health (anxiety and depression). Table 2 and 3 describes the anxiety level of patients in each period.

Table 2. Anxiety and Depression Level Characteristics of Patients in Each Period

Period (Week-)	Anxiety Level	Total Patients	Percentage	Depression Level	Total Patients	Percentage
0	Normal	16	26.7%	Normal	14	23.3%
	Borderline	28	30.0 %	Borderline	21	35.0%
	Anxiety Problem	26	43.3%	Depression Problem	25	41.7%
2	Normal	21	35.0%	Normal	17	28.3%
	Borderline	19	31.7%	Borderline	23	38.3%
	Anxiety Problem	20	33.3%	Depression Problem	20	33.3%
4	Normal	22	36.7%	Normal	15	25.0%
	Borderline	21	35.0%	Borderline	18	30.0%
	Anxiety Problem	17	28.3%	Depression Problem	27	45.0%
6	Normal	21	35.0%	Normal	15	25.0%
	Borderline	15	25.0%	Borderline	19	31.7%
	Anxiety Problem	24	40.0%	Depression Problem	26	43.3%
8	Normal	19	31.7%	Normal	14	23.3%
	Borderline	18	30.0%	Borderline	16	26.7%
	Anxiety Problem	23	38.3%	Depression Problem	30	50.0%
10	Normal	28	46.7%	Normal	14	23.3%
	Borderline	14	23.3%	Borderline	16	26.7%
	Anxiety Problem	18	30.0%	Depression Problem	30	50.0%
12	Normal	18	30.0%	Normal	16	26.7%
	Borderline	23	38.3%	Borderline	21	35.0%
	Anxiety Problem	19	31.7%	Depression Problem	23	38.3%
14	Normal	18	30.0%	Normal	13	21.7%
	Borderline	19	31.7%	Borderline	26	43.3%
	Anxiety Problem	23	38.3%	Depression Problem	21	35.0%

16	Normal	16	26.7%	Normal	18	30.0%
	Borderline	22	36.7%	Borderline	20	33.3%
	Anxiety Problem	22	36.7%	Depression Problem	22	36.7%
18	Normal	22	36.7%	Normal	13	21.7%
	Borderline	12	20.0%	Borderline	14	23.3%
	Anxiety Problem	26	43.3%	Depression Problem	33	55.0%
20	Normal	14	23.3%	Normal	13	21.7%
	Borderline	22	36.7%	Borderline	20	33.3%
	Anxiety Problem	24	40.0%	Depression Problem	27	45.0%
22	Normal	12	20.0%	Normal	15	25.0%
	Borderline	18	30.0%	Borderline	16	26.7%
	Anxiety Problem	30	50.0%	Depression Problem	29	48.3%
24	Normal	17	28.3%	Normal	16	26.7%
	Borderline	19	31,7%	Borderline	20	33.3%
	Anxiety Problem	24	40.0%	Depression Problem	24	40.0%

The first step of the data analysis in splitting the data into training and testing data (Nemesure, et al.., 2021) to perform prediction using GLMM and GNMM. To perform GLMM, the model is made based on the training data. Next, the testing data is used to evaluate the model's ability to generalize from training data to new data and assess its performance. The normality test for random effect residual is conducted using Shapiro-Wilk test and resulting $W = 0.994$ with $p - value = 0.888$, indicating that the residual is normally distributed.

To perform GNMM, λ and η are tuned using a validation set. The one-layer GNMM is trained using η = 0.005 and λ = 0.001 for both anxiety and depression levels, while the two-layer GNMM is trained using η = 0.005 and λ = 0.002 for both anxiety and depression levels. Furthermore, we conduct a leave-one-out cross validation only on the last observation for each patient since we are interested in predicting the anxiety and depression level outcome and compare the MSPE. Hu, et al. (2022) described that There are few references about how to measure the predictive power of methods in longitudinal data. The prediction accuracy according to a cross-validation method are not reasonable. The consideration for using the leave-one-out cross validation in this study is based on Geroldinger, et al.. (2023) stated that leave-one-out cross validation is a choice when analyzing longitudinal data with a small sample.

To determine the performance of GNMM in predicting the anxiety and depression levels of patients with pulmonary tuberculosis, we compare the results with the classical GLMM method. We use the shallow network architecture in this study due to a small sample size. Mandel, et al.. (2021) stated that large networks are used to model highly complex systems with high-dimensional data. In studies with small data, shallow models are more appropriate due to the presence of fewer training observations. Table 2 contains the MSPE comparison for the 6 models of anxiety and depression levels.

Table 3. MSPE Comparison of GLMM, 1-layer GNMM, and 2-layer GNMM

	GLMM	1-Layer GNMM	2-Layer GNMM
Anxiety	0.0321	0.0067	0.0075
Depression	0.0775	0.0071	0.0002

Based on Table 3, GNMM generally outperforms the classical GLMM. In addition to this, Jiang et al.. (2022) demonstrated the superiority of machine learning over traditional methods for longitudinal data analysis. The two-layer GNMM exhibits superior performance in forecasting anxiety and depression levels among patients with pulmonary tuberculosis, with an MSPE of 0.0075 and 0.0002 for anxiety and depression, respectively, which is the smallest among other methods. The GNMM with a single layer has a similar MSPE for anxiety and depression.

The two-layer GNMM accurately predicted anxiety and depression levels with a range score of 1.36-17.02. This was compared to the actual data, which had a range score of 0-19 for anxiety levels and a range score of 1.23-16.73 for depression levels. The actual data had a range score of 0-18 for depression. Careful consideration of their future mental health status can aid in monitoring and evaluating disease progression and in providing appropriate treatments based on levels of anxiety and depression.

5. CONCLUSION

Research on analyzing longitudinal data in healthcare is crucial for comprehending disease progression, assessing treatment effectiveness, and monitoring patient outcomes. Moreover, evidence indicates that mental health has an impact on disease outcomes, emphasizing the significance of suitable treatment. This specific investigation aimed to forecast the mental health needs of psychiatric patients in the upcoming period. The comparison of the three methods showed that the GNMM with two layers produced the most accurate prediction value. Future research should explore data with larger sample sizes or high-dimensional data with large network architectures to establish the robustness of GNMM.

ACKNOWLEDGMENT

The authors want to express their appreciation to all people who were involved in this study, including the partner, for their contribution to this writings

REFERENCES

Agbeko, C.K., Ali Mallah, M., He, B., Liu, Q., Song, H., & Wang, J. (2022). Mental Health Status and Its Impact on TB Treatment and Its Outcomes: A Scoping Literature Review. Frontier in Publich Health, 10, 1-12.

Breslow, N.E. & Clayton, D.G. (1993). Approximate Inference in Generalized Linear Mixed Models. Journal of the American Statistical Association, 88, 9-25.

Cascarano, A., Mur-petite, J., Hernández-González, J., Camacho, M., De Toro Eadie, N., Gkontra, P., Chadeau-Hyam, M., Vitrià, J., & Lekadir, K. (2023). Machine and Deep Learning for Longitudinal Biomedical Data: A Review of Methods and Applications. Artificial Intelligence Review (https://doi.org/10.1007/s10462-023-10561-w), 1-61.

Diggle, P.J., Liang, Y.K., & Zeger, S.L. (2006). Analysis of Longitudinal Data, Second Edition. New York: Oxford.

Efron, B. (2020). Prediction, Estimation, and Attribution. *Journal of the American Statistical Association, 115*(530), 636-655.

Fitzmaurice, G. M., Laird, N. M., & Ware, J. H. (2004). *Applied Longitudinal Analysis.* New Jersey: John Wiley& Sons, Inc.

Geroldinger, A., Lusa, L., Nold, M., & Heinze, G. (2023). Leave-one-out cross-validation, penalization, and differential bias of some prediction model performance measures—a simulation study. *Diagnostic and Prognostic Research*, 1-11.

Gumantan, A., Aditya, M., Imam, Y., & Rizki. (2020). Tingkat Kecemasan Seseorang Terhadap Pemberlakuan New Normal dan Pengetahuan terhadap Imunitas Tubuh. *Sport Science and Education Journal*, 18-27. doi:10.33365/ssej.v1i2.718

Hanusz, Z., & TarasiŃska, J. (2014). Simulation Study on Improved Shapiro–Wilk Tests for Normality. *Communications in Statistics - Simulation and Computation*, 2093-2105.

Hayward, S.E., Deal, A., Rustage, K., Nellums, L.B., Sweetland, A.C., Boccia, D., Hargreaves, S., & Friedland, J. S. (2022). The Relationship Between Mental Health and Risk of Active Tuberculosis: A Systematic Review. *BMJ Open, 12:e048945*.

Hu, S., Wang, Y.G., Drovandi, C., & Cao, T. (2022). Predictions of Machine Learning with Mixed-effects in Analyzing Longitudinal Data under Model Misspecification. *Statistical Methods & Applications*, 681-711.

Jiang, Z., Sheetal, A., & De Millia, L. (2022). Using Machine Learning to Analyze Longitudinal Data: A Tutorial Guide and Best-Practice Recommendations for Social Science Researchers. *Journal of Applied Psychology, 72*(3), 891-1364.

Lara-Espinosa, J.V. & Hernández-Pando, R. (2021). Psychiatric Problems in Pulmonary Tuberculosis: Depression and Anxiety. *Journal of Tuberculosis Research, 9*(1), 31-50.

Mandel, F., Ghosh, R.P., & Barnett, I. (2021). Neural Networks for Clustered and Longitudinal Data Using Mixed Effects Models. *Biometrics, 79*, 711-721.

Moynihan , K.M., Ziniel, S.I., Johnston, E., Morell, E., Pituch, K., & Blume, E. D. (2022). A "Good Death" for Children with Cardiac Disease. *Pediatric Cardiology*, 744-755. doi:10.1007/s00246-021-02781-0

Nemesure, M.D., Heinz, M.V., Huang, R., & Jacobson, N.C. (2021). Predictive Modeling of Depression and Anxiety Using Electronic Health Records and A Novel Machine Learning Approach with Artificial Intelligence. *Science Report*, 1-9.

Poli, I. & Jones, R.D. (1994). A Neural Net Model for Prediction. *Journal of the American Statistical Association, 89*(425), 117-121.

Rahmi, N., Medison, I., & Suryadi, I. (2017). Hubungan Tingkat Kepatuhan Penderita Tuberkulosis Paru dengan Perilaku Kesehatan, Efek Samping OAT dan Peran PMO pada Pengobatan Fase Intensif di Puskesmas Seberang Padang September 2012 - Januari 2013. *Jurnal Kesehatan Andalas*, 345-350. doi:10.25077/jka.v6i2.702

Rohmaniah, S. A., & Chandra, N. E. (2018). *Pemodelan Mortalita dengan Pendekatan GLMM.* Lamongan: Penerbit Pustaka Ilalang.

RSSA (2022). *Data Pasien Tuberkulosis Paru.* Malang: Rumah Sakit Saiful Anwar.

Rudy, M., Widyadharma, P.E., & Adnyana, I.M. (2015). Reliability Indonesian Version of The Hospital Anxiety and Depression Scale (HADS) of Stroke Patients in Sanglah General Hospital Denpasar.

Suryani, Widianti, E., Hernawati, T., & Sriati, A. (2016). Psikoedukasi Menurunkan Tingkat Depresi, Stres dan Kecemasan pada Pasien Tuberkulosis Paru. *Jurnal Ners, 11*(1), 128-133. doi:10.20473/jn.v11i1.1455

Verbeke, G. & Molenberghs, G. (2000). *Linear Mixed Model for Longitudinal Data.* New York: Springer Series in Statistics.

Wang, X., Li, X., Zhang, Q., Zhang, J., Chen, H., Xu, W., Fu, Y., Wang, Q., Kang, J., & Hou, G. (2018). A Survey of Anxiety and Depressive Symptoms in Pulmonary Tuberculosis Patients With and Without Tracheobronchial Tuberculosis. *Frontiers in Psychiatry, 9*(308), 1-10.

WHO (2022). *Global Tuberculosis Report 2022.* Geneva: World Health Organization.

Wu, H. & Zhang, J.T. (2006). *Nonparametric Regression Methods for Longitudinal Data Analysis.* New Jersey: John WIley and Sons, Inc.

Zigmond, A.S. & Snaith, R.P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67*(6), 361-370.