



ORIGINAL ARTICLE

Application of Mahalanobis-Taguchi System in Full Blood Count of Methadone Flexi Dispensing Program

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Abstract

Patient under methadone flexi dispensing (MFlex) program are required to do blood tests like full blood count (FBC). A doctor assesses 3 parameters like haemoglobin, platelet count, and fasting blood sugar to ensure the patient has FBC problem. The existing system does not have a stable ecosystem towards classification and optimization. The objective of this study was to apply Mahalanobis-Taguchi system (MTS) in the MFlex program. The data was collected at Bandar Pekan clinic with 34 parameters in the blood tests where 17 parameters in FBC, 8 parameters in liver function profile, 4 parameters in lipid profile, and 5 parameters in renal profile. Two types of MTS methods were used like RT-Method and T-Method for classification and optimization, respectively. As a result, the average Mahalanobis distance (MD) of healthy and unhealthy are classified using RT-Method with 1.00 and 187.06 respectively. Moreover, the significant parameters are evaluated using T-Method with 10 parameters of positive degree of contribution. 15 unknown samples have been diagnosed using MTS by using different positive and negative degree of contribution values to achieve lower MD. Type 2 of 6 modifications has been selected as the best proposed solution as it shows the highest MD value than others which is nearest to the positive value. In conclusion, a pharmacist from Bandar Pekan clinic admitted that MTS is able to solve problems in classification and optimization of MFlex program.

Keywords: Mahalanobis-Taguchi system; Mahalanobis distance; optimization; full blood count

Introduction

Drug addiction remains one of the big psychological, legal, and public health issues of the globalized era (REF). About 35 million people are estimated to suffer from substance use problems and need recovery facilities (Bewley-Taylor & Nougier, 2018). A study published by the United Nations Office on Drugs and Crime (UNODC) stated that the opioid users are 53 million, up 56% from previous reports, and that opioids are accounting for two-thirds of the 585,000 people who died as a factor of drug usage in 2017 (Vienna, 2019). Several factors contribute to drug abuse involvement. One of the factors is the influence of peers. In addition, parents are also a

factor for children to be involved drug addicts (Buntat & Rahaman, 2014). From 2014 to 2018, National Anti-Drugs Agency (NADA) detected a total of 116,206 addicts with 73.6% of them which is 85,575 people consisting of youths aged 19 to 39 years (Hassan, 2020). The implementation of the MFlex program has generally proven to be effective in HIV/AIDS issues and billing. The program managed to improve the life of this drug addict. Methadone treatment is given daily as an outpatient. Participation in the MFlex program can also be a platform for patients to detect problems other health such as HIV, hepatitis, and TB. Percentage of new HIV cases as a result injection drug addiction reported to the Ministry of Health has shown a significant decrease from 66% with 4,038 cases in 2005 to 16.8% with 561 cases on 2015 (Yuswan & Dazali, 2016). MTS is used to create reference scales by generating individual scales of measurement for each parameter (Jobi-Taiwo & Cudney, 2015). Patient under MFlex program are required to do 4 types of blood tests, such as FBC, liver function profile, lipid profile, and renal profile involving 34 parameters to determine whether the patient has other diseases or vice versa. In addition, to ensure if the patient has FBC problem, a doctor is required to assess 3 parameters such as haemoglobin (HGB), platelet count (PLT), and fasting blood sugar. This proves that the existing system does not have an accurate measurement method and lack of justification of significant parameters.

The objective of this research was to analyse the classification and optimization factors in the FBC, and to diagnose the unknown data of the MFlex program. Literature review describes related studies on MTS, where the research gap on MTS is the most significant in this chapter. Next, research methodology explains the methods and strategies used to meet the goal or objectives of the research. Result and discussion elaborate all the evidence that has been possessed during data collection using the MTS method for classification and optimization. Lastly, the conclusion concludes the final findings after the measurements have been handled and provides some recommendations for the subsequent work.

About 270 million individuals or about 5.5% of the world population aged 15-64 had used psychoactive medications and an estimated 35 million individuals impacted by substance abuse problems which is a dangerous pattern of opioid use or dependency. It is reported that opioid use causes about 0.5 million deaths per year, including about 350 000 male and 150 000 female deaths (World Health Organization, 2019).

Table 1 shows the number of opioid dependents classified by case status from 2013 to 2018. A total of 25,267 opioid dependents were detected in 2018, reflecting a decline of -2.5% or 25,922 drug dependents relative to the same period in 2017. They consisted of 17,474 new opioid dependents, a decline of -5.2% relative to 18,440 during the same duration in 2017 (Ministry, 2019).

Table 1. Amount of opioid dependents by case status in Malaysia, 2013-2018

Year	Amount of opioid dependents		Total
	New	Relapse	
2013	13,481	7,406	20,887
2014	13,605	8,172	21,777
2015	20,289	6,379	26,668
2016	22,923	7,921	30,844
2017	18,440	7,482	25,922
2018	17,474	7,793	25,267

The government has implemented MFlex program which is one of the components of harm reduction in October 2005 in the country's efforts to address HIV/AIDS among injecting drug users and at the same time address the issue of opiate addiction, especially heroin in Malaysia. Methadone was used in the treatment of heroin addiction in the mid-1960s and has proven to be safe and effective. This program has also proven to be effective in reducing the incidence of HIV

due to injectable drug addiction and crime incidents among this target group (Yuswan and Dazali, 2016).

Mahalanobis Taguchi System by Genichi Taguchi is the implementation of the Taguchi Methods concepts in multivariate applications that helps in quantitative decision making by constructing a multivariate scale of measurements using a data-analytical process (Taguchi, 2001). In MTS, the Mahalanobis space (MS) is accomplished by calculating uniform variables of healthy or normal data. The MS could be used to differentiate between normal and abnormal items. When this MS is defined, the number of features is decreased using the orthogonal array (OA) and the signal-to-noise ratio (SNR) by measuring the input of each attribute (Cudney et al., 2006).

Mahalanobis distance was first proposed in 1930 by PC Mahalanobis. It is a useful tool for establishing the similarities between an unknown data set and a known data set. There are two major variations in the distance between the MD and the Euclidian distance (ED) as shown in Figure 1. The similarity between data is maintained with the MD and the reliance of the measurement scale is classified with the MD. It should be remembered that the number of variables in the method does not influence the calculated MDs. In addition, MD is very sensitive to changes in the reference data. These are MD's superiorities to other distances in multidimensional space (Ghasemi et al., 2015).

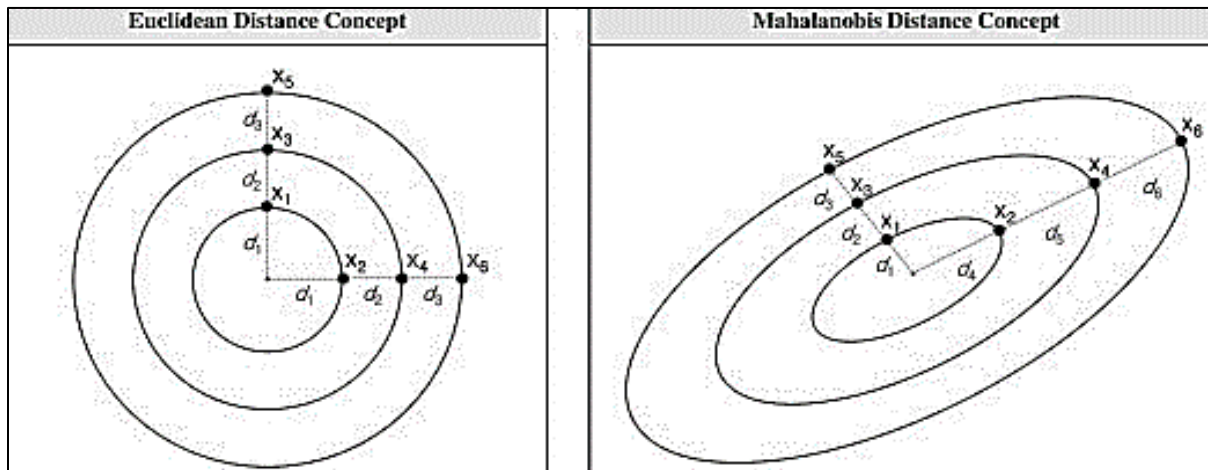


Figure 1. Comparison between MD and ED.

RT-Method is used in the MTS for classification problem. The “Unit Space” is described by the RT-Method, and the distance from its center to the object data is measured as MD. The disparity between the RT-Method and the multivariate control chart has been said to be difficult to understand due to some mathematical features shared by both. Nonetheless, the RT-Method and the multivariate control chart vary greatly in terms of objective and technical organization (Teshima et al., 2012). The distinctions in concepts and organizational techniques between RT-Method and multivariate control chart is shown in Table 2.

Table 2. The distinctions in concepts and organizational techniques

Concept and Organizational Technique	RT-Method	Multivariate Control Chart
Differences in the definition of normalcy	To provide reliable identification, Unit Space is established using homogeneity (normal state, state of consistency, state of high concentration) concerning the aim as the benchmark.	It considers the normal condition to be the standard and finds no relevance in the presence or absence of the homogeneity component.

Technique proposal for feature extraction	The effectiveness of feature extraction in pattern recognition impacts the outcome of the entire process.	No concept such as feature extraction is used, and the observed data is used in a nearly raw form.
Proposal for a recognition system evaluation criterion	<ul style="list-style-type: none"> - Includes a concept for quantifying success/failure in the recognition system. - The SN ratio can be used to assess the overall suitability of a recognition system. 	NIL
Item selection proposal	<ul style="list-style-type: none"> - Choose a variable that is efficient for detecting abnormalities. - Remove unneeded variables to increase the sensitivity of anomaly detection. 	There are no such recommendations with the multivariate control chart.
Proposal for a diagnostic method for abnormality causes	<ul style="list-style-type: none"> - When an abnormality event happens, the causes can be identified. - When target data (unknown data) is found to be abnormal, it is feasible to establish which variable is generating the anomaly. 	NIL

T-Method is used in the MTS for optimization problem. A theory that predicts and estimates an outcome value (objective variable) dependent on a multivariate, and it serves the same function as multiple regression analysis. However, the analytical processes vary significantly (Teshima et al., 2012). In this section, we will look at what distinguished T-Method from multiple regression analysis. The differences between T-Method and multiple regression analysis are summarized in **Table 3**.

Table 3. Comparison of T-Method and multiple regression analysis

	T-Method	Multiple
Unit Space	Selection is made from a homogenous, dense population with a median range output value.	The concept of "Unit Space" was not accepted. The total amount of data utilized to construct the regression formula.
Conditions restrictive	<ul style="list-style-type: none"> - The number of samples of Unit Space $n \geq 1$. - The number of samples of Signal Data $1 \geq 2$. - (There is no multicollinearity.) 	<ul style="list-style-type: none"> - The restriction is that the total number of items $n >$ number of items k. - If multicollinearity exists, no solution is available. The removal of items may make it possible, but the effects of significant items may become hard to identify.
Correlation between elements	<ul style="list-style-type: none"> - Correlation between elements that were <i>not</i> used. - Signal Data outputs and items are subjected to a single regression (proportional equations with a reference point of zero). - If the correlation is near to "1", the accuracy of the integrated estimate value may affect. 	<ul style="list-style-type: none"> - Correlation between elements that were used. - If the correlation is near to "1", partial regression coefficients and a single regression coefficient's signs will not correspond.
The accepted evaluation function	SN ratio η integrated estimate	Multiple correlation coefficient, often known as multiple correlation coefficient corrected for degrees of freedom.

There are some advantages of MTS such as it allowed to identify of abnormalities even though learning data were classified as 'unlabelled' (Ohkubo and Nagata, 2019), it used to create a continuous scale of measurement and to calculate the abnormality degree (Chang et al., 2019), and it measures healthy retrospective observations and unhealthy retrospective observations (Buenviaje et al., 2016). On the other hand, MTS can handle issues with binary classification only (Wang et al., 2018), characteristic factors may show the covariance matrix and multicollinearity is singular and irreversible which is MD cannot be calculated in this way (Chen et al., 2018), and it lacks a strategy for evaluating an appropriate binary classification threshold (El-Banna, 2017).

According to Figure 2, there are several applications used in the MTS method. There are 9 types of applications such as, mechanical, automotive, institutions, healthcare, case study, software, classification, manufacturing, and agriculture. The pie chart is obtaining from 104 published work from 2011 to 2020. Among them, the manufacturing sector is the most work performed by the MTS process, which had the highest percentage of 22%, with 23 from 104 research articles. Meanwhile, agriculture has had the lowest rate, which is 1% for the application sector which is only 1 research article that used the MTS process. The percentage for mechanical, automotive, institutions, healthcare, case study, software, and classification are 14%, 6%, 10%, 9%, 8%, 11%, and 19% respectively. This proves that MTS is widely used in the manufacturing sector such as maintenance outsourcing process, remanufacturing crankshaft, cutting tool wear, tablet PC production processes, bearing fault, welding faults, and many more.

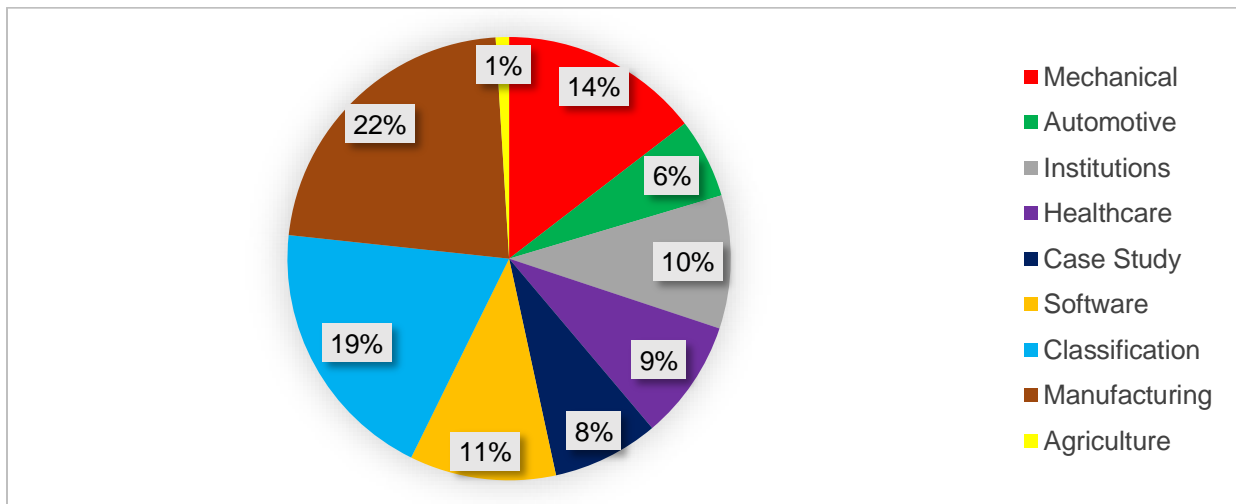


Figure 2. Application of MTS.

According to Mota-Gutiérrez et al. (2018), the research of MTS is qualified into 7 categories which are, introduction to the method, case of study/application, comparison with other methods, construction of MS, integration, and development with other methods, dimensional reduction, and threshold establishment. This work is used these categories to summarize the research gap of the published work from the year 2011 to 2020 as shown in Figure 3. It can be seen that the integration and development with other methods had the highest percentage of 26% for the application fields using MTS. Then, followed by threshold establishment with 22%, dimensional reduction with 18%, comparison with other methods with 15%, case study/application with 8%, introduction to the method with 6%, and construction of MS with 5%.

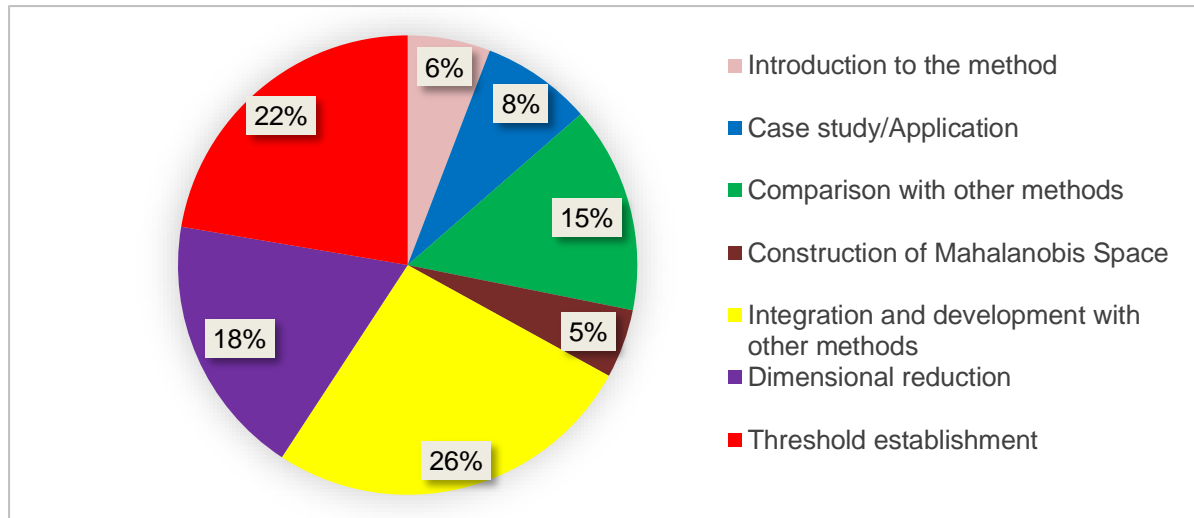


Figure 3. Variety of application field in MTS.

The highest percentage which contribute 26% in integration and development with other methods stated the MD dependent on the Minimum Regularized Covariance Determinants (MRCDD) estimator measured in high-dimensional data sets (Bulut, 2020). MD and Decision Tree (DT) examined abnormal activity patterns (Chen et al., 2020). The updated MTS as amended by the Fischer Linear Discriminant Analysis (FLDA) used to understand the operating condition of the machinery (Wang et al., 2019). Globally Harmonized System (GHS) and the MTS had overcome such limitations of chemical management have solved the shortcomings of chemical control (Lim et al., 2019). The combination of MTS and a hybrid binary metaheuristic based on particle swarm optimization and gravitational search algorithm (BPSOGSA) conducted an optimum set of features in order to detect the related variables in the actual phase of foam injection in the automotive industry (Reséndiz-Flores et al., 2019). An indirect conventional Mahalanobis distance-based approach (ICMD) has found outliers and significant points (Liu et al., 2018). The Random Binary Search (RBS) method in MTS enhanced the collection of the most useful variables (Muhamad et al., 2018). Besides, MTS forecast the conditions of the dynamic structure of the chemical industry (Lv and Gao, 2011), sensed various degrees of fault and identified specifically using vibration signals (Ren et al., 2011). The MD presented useful knowledge in the goals and background statistics (Imani, 2018), observed abnormal work environment during the production of the product (Campora et al., 2017), and measured the distance between each investment program and the optimal programs (Li et al., 2016). The integration of the U-statistic and MD techniques isolated geochemical anomaly from the history (Ghannadpour and Hezarkhani, 2017). The MD, and multiple regression analysis measured the output difference and the implicit significance of value characteristics (Ho et al., 2016). Laplacian MTS (LMTS) developed a nonlinear mapping correlation of the sensor information and the output of the ball screw (Zhao et al., 2016).

Functional Mahalanobis semi-distance has produced new variants of many well-known functional classification techniques (Galeano et al., 2014). MTS and logistic regression (LR) models have minimized query items (Lee et al., 2014). MTS, and self-organization mapping (SOM) network, called the MTS-SOM method, distinguish the incipient fault state and monitor the complex deterioration pattern of running bearings through observations of real-time vibration (Hu et al., 2013). MTS using an adaptive resonance theory neural network (ARTN) approach solved the collection of parameters in a dynamic product design scheme (DPDS) (Huang et al., 2013). MTS with Two-Step Optimal (TSO) approach has solved parameter choices in a complex setting for product design optimization (Huang et al., 2013). The key characteristics were calculated by the MTS-based diagnostic system (Wang et al., 2012). The combination of MTS and cluster analysis methodology defined the most suitable training package, identified and utilized to well-

known datasets in order to test the failure of the software systems (Liparas et al., 2012). The frequency of ulcer pressure was estimated by MTS, Support Vector Machines (SVMs), DT and LR (Su et al., 2011).

Abu et al. (2014) applied MTS to the big-end diameter of connecting rod to distinguish between two distinct ranges within the remanufacturability process spectrum. Abu and Jamaludin (2014) provided a systematic analysis of the data set on the main journal diameter of crankshaft. Abu et al. (2015) provided a systematic pattern recognition using MTS by constructing a scatter diagram which could support decision making of particular industry on 14 main journals of crankshaft belong to 7 engine models with different numbers of samples. Abu et al. (2017) classified crankshafts' end life into recovery operations based on the Mahalanobis-Taguchi system. Nik Mohd Kamil and Abu (2018) developed a distinctive pattern of crankshaft and identify the critical and non-critical parameter of crankshaft based on the MTS, then applied the Activity Based Costing (ABC) as a method of estimation for the remanufacturing cost of crankshaft. Abu et al. (2018) identified the critical and non-critical variables during remanufacturing process using MTS and simultaneously estimate the cost using ABC method. Abu et al. (2018) evaluated the criticality of parameters on the end of life crankshaft based on Taguchi's orthogonal array. Then, estimate the cost using traditional cost accounting by considering the critical parameters. Azmi et al. (2019) measured the degree of abnormality using MTS and diagnosed the parameters that influence the system. Nik Mohd Kamil et al. (2020) proposed of MTS and Time-Driven Activity-Based Costing (TDABC) in electric and electronic industry to evaluate the significant parameters and develop time equation and capacity cost rate respectively. Nik Mohd Kamil et al. (2020) identified 4 insignificant and 11 significant parameters in the visual mechanical inspection workstation using MTS. Safeiee et al. (2020) found that positive gain through SNR indicates the quality of system still in good condition from February with 0.1244 until December with 0.4432 after insignificant variable has been removed using MTS. Kamil et al. (2021) concluded that MTS is a practical method for classification and optimization in the industry. Kamil et al. (2021) concluded that MTS and TDABC are a great tool and feasible to be implemented in the electronic industry. Saad et al. (2021) developed MTS based graphical user interface for analyzing and classifying the normal and abnormal patient under MFlex service for better monitoring system. Ramlie et al. (2021) concluded that none of the four thresholding methods outperformed one over the others in (if it is not for all) most of the datasets. Harudin et al. (2021) proved that incorporating Bitwise Artificial Bee Colony (BitABC) techniques into Taguchi's T-Method methodology effectively improved its prediction accuracy.

Materials and Methods

This research work focused on MFlex program under Ministry of Health Malaysia in the blood tests. The 34 parameters of blood tests are defined into four types namely, FBC, liver function profile, lipid profile, and renal profile that were used to identify the healthiness of methadone patients. Four types of the diseases are for the classification of the methadone patients whether they had one of the diseases in those four types during joining the MFlex program. Moreover, the significant parameters of the blood tests can be optimized. Table 4 shows the parameters of blood tests which contain 34 parameters selection and reference range which classify as healthy group. The parameters for FBC, liver function profile, lipid profile, and renal profile are 17, 8, 4, and 5 respectively.

Table 4. Parameters in blood tests

Parameters	Unit	Reference range
Full Blood Count (FBC)		
1. White Blood Cell (WBC)	10 ⁹ /L	(4.0-11.0)

2. Red Blood Cell (RBC)	10 ¹² /L	(3.5-5.6)
3. Haemoglobin (HGB)	g/dL	(11.5-16.4)
4. Hematocrit (HCT)	%	(36-47)
5. Mean Corpuscular Volume (MCV)	fL	(76-96)
6. Mean Corpuscular Haemoglobin (MCH)	pg	(27-32)
7. Mean Cell Haemoglobin Concentration (MCHC)	g/dL	(30-35)
8. Platelet Count (PLT)	10 ⁹ /L	(150-400)
9. Lymphocyte % (LYM%)	%	(20.0-45.0)
10. Lymphocyte # (LYM#)	10 ⁹ /L	(1.5-3.5)
11. MXD %	%	(3.0-10.0)
12. MXD #	10 ⁹ /L	(2.0-7.7)
13. NEUT %	%	(40.0-75.0)
14. NEUT #	10 ⁹ /L	(2.5-7.5)
15. MPV	fL	(5.0-10.0)
16. PDW	fL	(12.0-18.0)
17. Fasting Blood Sugar	mmol/L	(4.1-5.9)
<i>Liver Function Profile</i>		
18. Total Protein	g/L	(65-85)
19. Albumin	g/L	(35-52)
20. Globulin	g/L	(20-39)
21. A/G Ratio	-	(0.9-1.8)
22. Total Bilirubin	umol/L	(2-24)
23. Alk Phosphatase	U/L	(30-115)
24. ALT (SGPT)	U/L	(0-41)
25. AST (SGOT)	U/L	(0-41)
<i>Lipid Profile</i>		
26. Cholesterol	mmol/L	(3.60-5.20)
27. Triglycerides	mmol/L	(0.50-2.00)
28. HDL Cholesterol	mmol/L	(0.90-1.55)
29. LDL Cholesterol	mmol/L	(2.3-4.4)
<i>Renal Profile</i>		
30. BUN	mmol/L	(1.7-8.5)
31. Creatinine	umol/L	(62-150)
32. Sodium	mmol/L	(135-152)
33. Potassium	mmol/L	(3.5-5.5)
34. Chloride	mmol/L	(95-114)

The RT-Method could classify items into two categories which are within and outside the unit space. Unit data was chosen on the basis of the largest number of samples, among other samples. The RT-Method measured value of the output, but the category is clear when more than one unit spaces exist. The average value for each parameter is calculated as shown in equation (1), from n number of samples in healthy group.

$$\bar{x}_j = \frac{1}{n}(x_{1j} + x_{2j} + \dots + x_{nj}) \quad (j = 1, 2, \dots, k) \quad (1)$$

The sensitivity β , the linear formula L , and the effective divider r , are shown in equation (2), equation (3), and equation (4) respectively.

$$\text{Sensitivity, } \beta_1 = \frac{L_1}{r} \quad (2)$$

$$\text{Linear equation, } L_1 = \bar{x}_1 x_{11} + \bar{x}_2 x_{12} + \dots + \bar{x}_k x_{1k} \quad (3)$$

$$\text{Effective divider, } r = \bar{x}_1^2 + \bar{x}_2^2 + \dots + \bar{x}_k^2 \quad (4)$$

The total variations S_T , variation of proportional term S_β , error variation S_e , and error variance V_e , are shown in equation (5), equation (6), equation (7), and equation (8) respectively.

$$\text{Total variation, } S_{T1} = x_{11}^2 + x_{12}^2 + \dots + x_{1k}^2 \quad (5)$$

$$\text{Variation of proportional term, } S_{\beta1} = \frac{L_1^2}{r} \quad (6)$$

$$\text{Error variation, } S_{e1} = S_{T1} - S_{\beta1} \quad (7)$$

$$\text{Error variance, } V_{e1} = \frac{S_{e1}}{k-1} \quad (8)$$

The standard SN ratio η is then calculated as stated in the equation (9). The greater the value of η , the stronger the relationship between the input and output.

$$\text{SN ratio, } \eta_1 = \frac{1}{V_{e1}} \quad (9)$$

The sensitivity β , and the standard SN ratio η , are then calculated in the healthy group, and the two variables Y_1 and Y_2 are calculated to generate a scatter diagram. The equation (10) and equation (11) show the value of Y_1 and Y_2 respectively.

$$Y_{i1} = \beta_i \quad (10)$$

$$Y_{i2} = \frac{1}{\sqrt{\eta_i}} = \sqrt{V_{ei}} \quad (11)$$

The prediction of origin is referred to the calculation of average for Y_1 and Y_2 in equation (12) and equation (13) respectively.

$$\bar{Y}_1 = \frac{1}{n} (Y_{11} + Y_{21} + \dots + Y_{n1}) \quad (12)$$

$$\bar{Y}_2 = \frac{1}{n} (Y_{12} + Y_{22} + \dots + Y_{n2}) \quad (13)$$

Finally, MD is calculated through equation (14).

$$\text{Mahalanobis distance, } D^2 = \frac{YA^{-1}Y^T}{k} \quad (14)$$

The methadone patients who are under monitoring was classified as unhealthy group. To calculate unhealthy group, the similar equation as healthy group is repeated, but the different between two groups is in normalization of unhealthy group. The linear equation L' , and the effective divider r' , are calculated as the same equation in healthy group which are equation (3) and equation (4) respectively. Note that the average values of samples and parameters \bar{x} , and the effective divider r' , are the same values of the healthy group. Next, the value sensitivity β , for each unhealthy group can be calculated as stated in the equation (2).

After that, the total variations S_T , variation of proportional term S_β , error variation S_e , and error variance V_e , are calculated through equation (5), equation (6), equation (7), and equation (8) respectively. The value of sensitivity β , and the standard SN ratio η , from unhealthy group are used for the calculation of variables Y_1 and Y_2 as well. The value of sensitivity β is used for Y_1 as stated in equation (10), meanwhile the variable Y_2 is converted first as stated in the equation (11)

for allowing the evaluation of any scattering from the normal conditions. The average value for Y_1 and Y_2 are same as shown in the equation (12) and equation (13) respectively for the prediction of healthy group origin. Lastly, the MD value can be found based on the equation (14).

The T-Method is utilized as evaluation to the parameters towards the output. The highest sample will be defined as a healthy group while remaining number of samples will be defined as unhealthy group. The average values for every parameter and the output average value from the number of samples in the healthy group are found as shown in equation (15) and equation (16) respectively.

$$\bar{x}_j = \frac{1}{n} (x_{1j} + x_{2j} + \dots + x_{nj}) \quad (15)$$

$$\bar{y} = m_0 = \frac{1}{n} (y_1 + y_2 + \dots + y_n) \quad (16)$$

The balance samples that belong to healthy group are defined as unhealthy group. After that, the unhealthy group has been normalized using the average value of every parameter and output that belong to healthy group. The aim of normalization is to make the data more flexible by removing their redundancy. The calculation of normalized data for input and output are shown in the equation (17) and equation (18) respectively.

$$X_{ij} = \acute{x}_{ij} - \bar{x}_j \quad (17)$$

$$M_i = \acute{y}_i - m_0 \quad (18)$$

Proportional coefficient β and SN ratio η for each parameter are calculated as shown in equation (19), equation (20), equation (21), equation (22), equation (23), equation (24), and equation (25).

$$\text{Effective divider, } r = M_1^2 + M_2^2 + \dots + M_l^2 \quad (19)$$

$$\text{Total variation, } S_{T1} = X_{11}^2 + X_{21}^2 + \dots + X_{l1}^2 \quad (20)$$

$$\text{Variation of proportional term, } S_{\beta_1} = \frac{(M_1 X_{11} + M_2 X_{21} + \dots + M_l X_{l1})^2}{r} \quad (21)$$

$$\text{Error variation, } S_{e1} = S_{T1} - S_{\beta_1} \quad (22)$$

$$\text{Error variance, } V_{e1} = \frac{S_{e1}}{l-1} \quad (23)$$

$$\text{Proportional Coefficient, } \beta_1 = \frac{M_1 X_{11} + M_2 X_{21} + \dots + M_l X_{l1}}{r} \quad (24)$$

$$\text{SN ratio, } \eta_1 = \begin{cases} \frac{\frac{1}{r}(S_{\beta_1} - V_{e1})}{V_{e1}} & (\text{when } S_{\beta_1} > V_{e1}) \\ 0 & (\text{when } S_{\beta_1} \leq V_{e1}) \end{cases} \quad (25)$$

A positive value of β means that the steepness is ascending to the right, while a negative value of β means that the steepness is descending to the right. The value of η should be in positive value, but if it turns out to be in negative value, it will be considered zero which means there is no longer a significant relationship between input and output.

The integrated estimate value of unhealthy group is computed by using the proportional coefficient β and SN ratio η for each parameter. The calculation of integrated estimate value is shown in equation (26). Note that, $x_{j1}, x_{j2}, \dots, x_{j6}$ are the normalized value of each parameter.

$$\text{Integrated estimate value, } \widehat{M}_i = \frac{\eta_1 \times \frac{x_{i1}}{\beta_1} + \eta_2 \times \frac{x_{i2}}{\beta_2} + \dots + \eta_k \times \frac{x_{i6}}{\beta_6}}{\eta_1 + \eta_2 + \dots + \eta_6} \quad (26)$$

The step by step for calculating estimated SN ratio η are using the following equation (27), equation (28), equation (29), equation (30), equation (31), equation (32), and equation (33). In fact, the estimated SN ratio η is based on the suitability of OA.

$$\text{Linear equation, } L = M_1 \widehat{M}_1 + M_2 \widehat{M}_2 + \dots + M_l \widehat{M}_l \quad (27)$$

$$\text{Effective divider, } r = M_1^2 + M_2^2 + \dots + M_l^2 \quad (28)$$

$$\text{Total variation, } S_T = \widehat{M}_1^2 + \widehat{M}_2^2 + \dots + \widehat{M}_l^2 \quad (29)$$

$$\text{Variation of proportional term, } S_\beta = \frac{L^2}{r} \quad (30)$$

$$\text{Error variation, } S_e = S_T - S_\beta \quad (31)$$

$$\text{Error variance, } V_e = \frac{S_e}{l-1} \quad (32)$$

$$\text{Estimated SN ratio, } \eta = 10 \log \left[\frac{\frac{1}{r}(S_\beta - V_e)}{V_e} \right] \quad (33)$$

The relative importance of parameter is evaluated in terms of the extent to which the estimated SN ratio deteriorates when the parameter is not used. Two-level OA which is level 1 and level 2 is used for an evaluation. The use of OA enables measurements to be made of the estimated SN ratio under various conditions. The two-level of OA means that level 1 is parameter will be used and level 2 is parameter will not be used. With respect to the estimated SN ratio, the difference between the averages of SN ratio for level 1 and level 2 for each parameter and on that basis determine the relative importance of the parameters. When the parameter is used with larger SN ratios and when the parameter is not used with smaller SN ratios, the degree of contribution turns to be positive. Otherwise, when the parameter is used with lower SN ratios and when the parameter is not used with higher SN ratios, the degree of contribution turns to be negative.

Results and Discussion

The scatter diagrams of the blood tests between healthy and unhealthy groups are created. All the unhealthy group are computed sample by sample through two variables of Y_1 and Y_2 . The y-axis represents Y_2 and the x-axis represents Y_1 . The blue dotted on the graph represent the healthy group with 50 samples while the orange dotted represent the unhealthy group. These graphs consist of 34 blood test parameters and the number of samples for the FBC is 30. Figure 4 shows a scatter diagram of FBC between healthy and unhealthy samples. The healthy and unhealthy samples form a different group of aggregation data. In other words, both samples form a classification through MD value. The minimum value of MD for healthy is 0.0111 and the maximum value of MD is 5.6593. Meanwhile, the minimum and maximum value of MD for

unhealthy are 103.1935 and 249.8483 respectively. This can be concluded that, there was no overlap between healthy and unhealthy samples because the range number of MD for both samples are distinctive. This has been proven that average MD for healthy is 1.0000 while the average MD for unhealthy is 187.0555. This confirm that both samples are not identical.

In addition, the correlation coefficient r for healthy samples (blue dotted) is 0.0585 which is nearer to zero. It means the relationship between the variable Y_1 and Y_2 is weak although technically it is a positive correlation. Meanwhile, the correlation coefficient r for unhealthy samples (orange dotted) is 0.9766. It means the variables have a strong positive correlation.

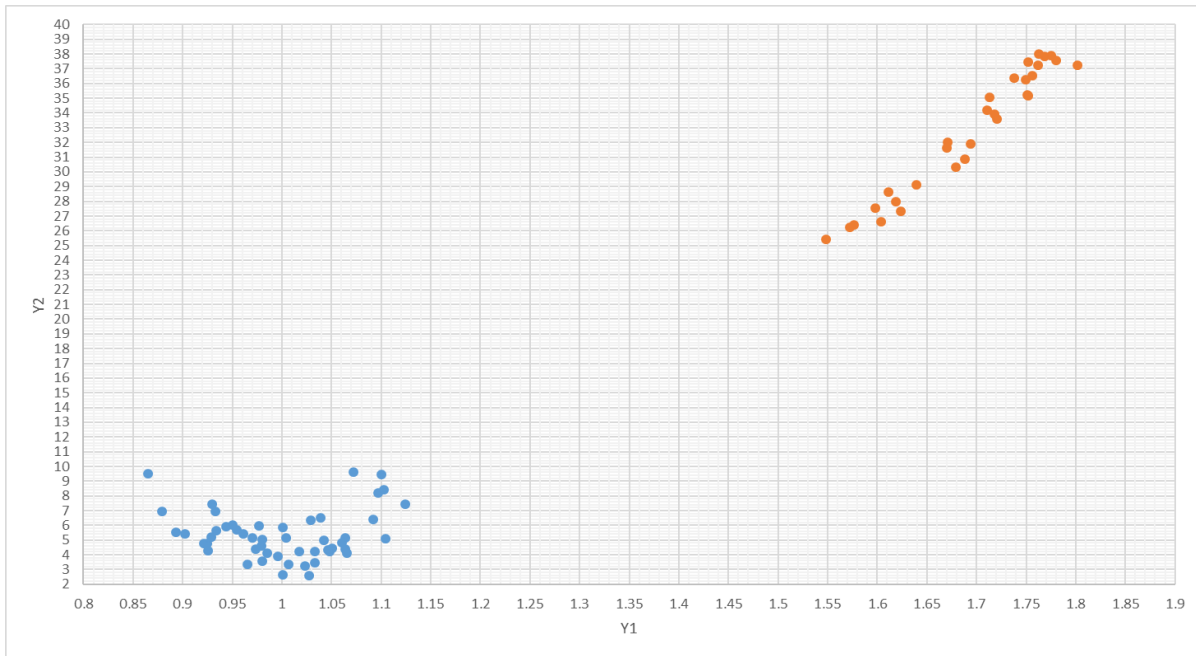


Figure 4. Scatter diagram of FBC between healthy and unhealthy.

In the FBC blood tests, the number of healthy and unhealthy samples are 5 and 75 respectively with 34 parameters. The data is organized in the ascending order of output value, as shown in Figure 5. Sample number 11 turns out to be the smallest with 0.011 while sample number 73 turns out to be the largest with 250.369. That means sample number 51, 64, 53, 63, and 76 are set to be the center point in blue and red dotted.

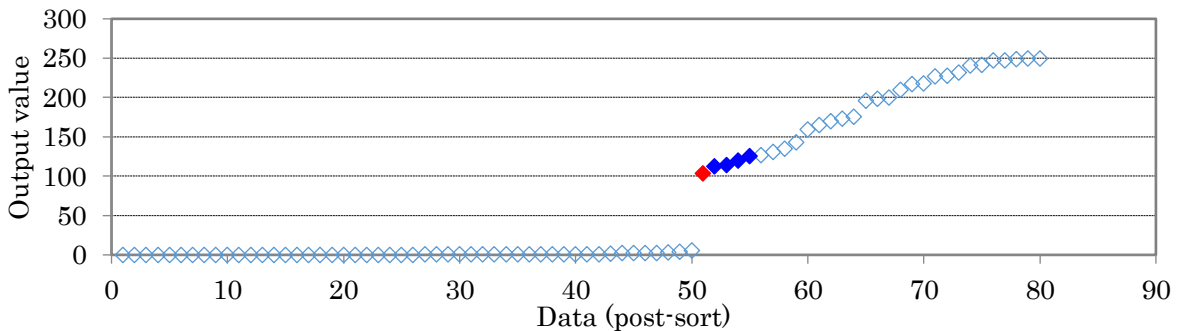
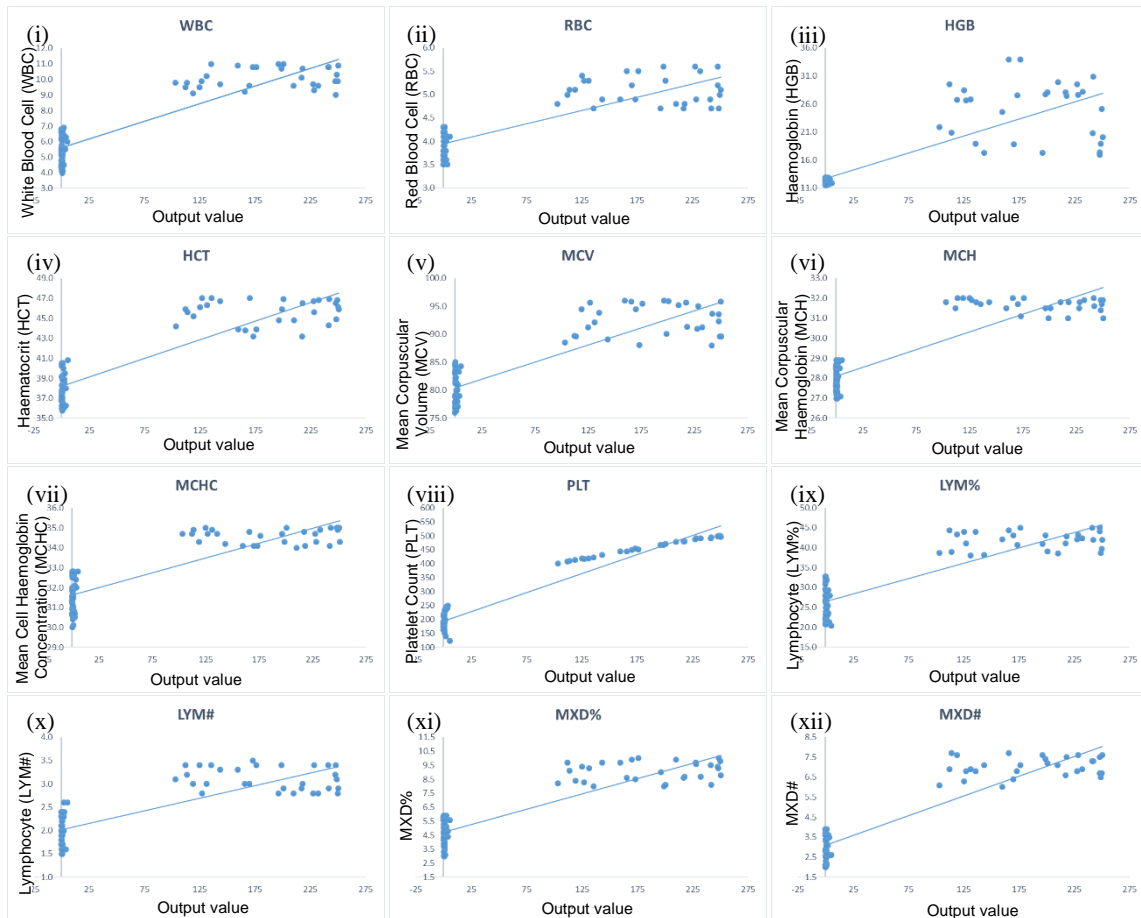


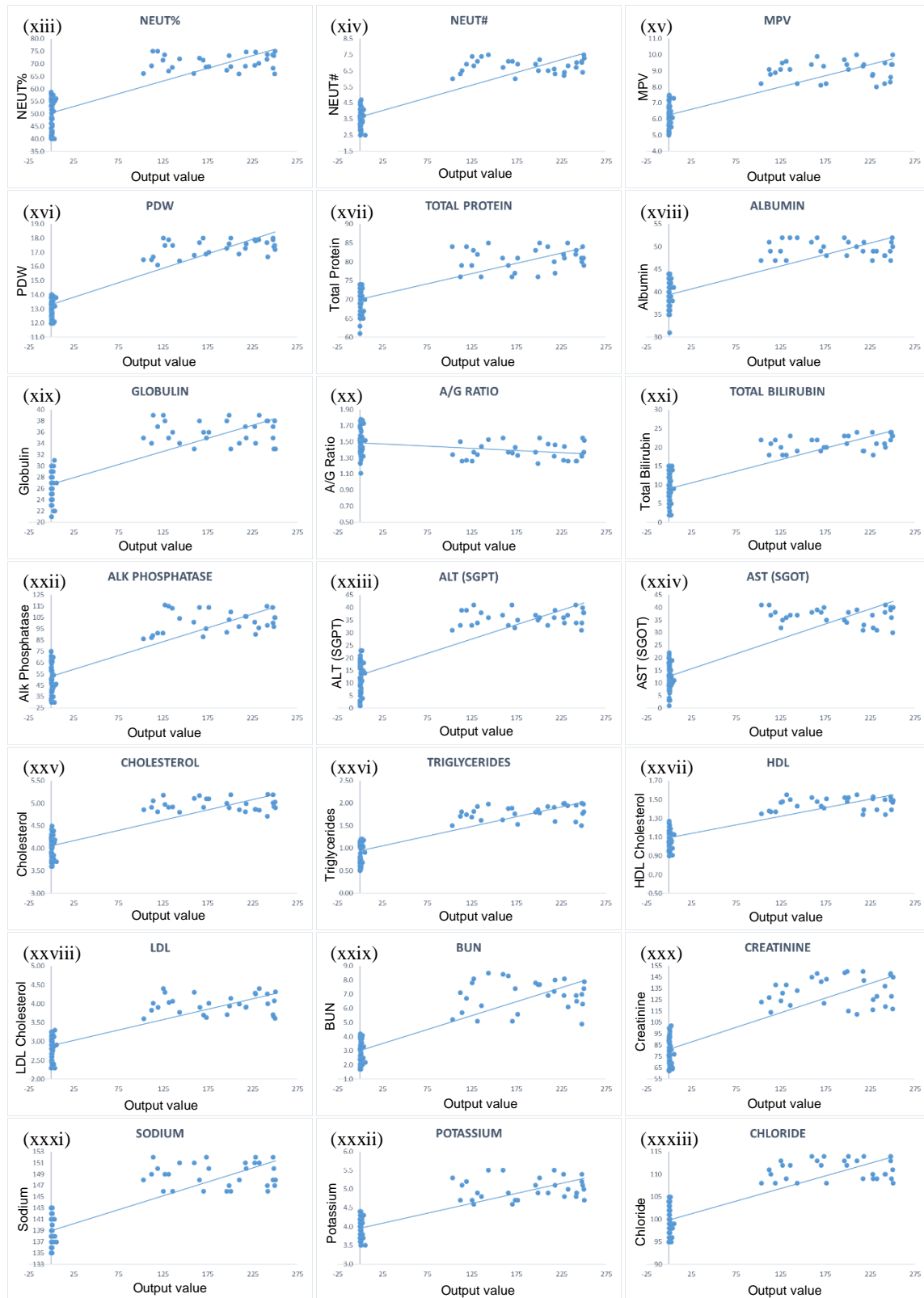
Figure 5. Data (post-sort) for FBC in blood tests.

The relationship between parameters and their output values is shown in Figure 6. The x-axis represents the normalized output values and the y-axis represents the normalized

parameters values. To determine which of the parameters would be useful for evaluation, parameter by parameter computation of the proportional coefficient β and SN ratio η were carried out. The T-Method calculates SN ratios η and proportional coefficients β based on the relationship between the normalized output value and the normalized parameter value. According to Teshima et. al (2012), the greater the SN ratios η produces a stronger relationship or in the other words the distribution is closer to a blue line. Since Figure 6 (iii) which represents the parameter of haemoglobin has 0.0002 SN ratio η , so the distribution is far away from a blue line whereas Figure 6 (viii) which represents the parameter of platelet count has 0.0006 SN ratio η , so the distribution is approaching to the blue line. This proves that the greater value of SN ratio, the closer the distribution to a blue line in a graph.

Furthermore, Teshima et. al (2012) also stated that ascending the line from left to the right indicates the parameter has a positive value of proportional coefficients β whereas the descending the line indicates the parameter has a negative value of proportional coefficients β . This has been proven through Figure 6 (xx) which represents the parameter of A/G ratio has -0.0009 of proportional coefficient β whereas the remaining 33 parameters has positive value of proportional coefficient β . As a result, those parameters are well suited to the purpose of calculating integrated estimate value. This study would derive the value of integrated estimate value by using those proportional coefficient β and SN ratios η values. Therefore, the higher the SN ratios η , the greater the degree to which it contributes to the integrated estimates of MD value which is closer to the actual normalized MD value. Since none of those parameters has a negative SN ratio η value, subsequently all those parameters are considered in integrated estimate value.





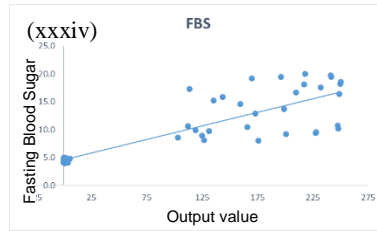


Figure 6. Scatter of normalized output and parameter values of FBC.

Figure 7 shows a scatter diagram reflecting of what happens when actual values are expressed in x-axis terms, and the estimated values in y-axis terms. If estimated values line up above a straight line, it indicates that a good estimation has been made. Furthermore, the graph will offer additional information regarding an approximate straight line and its attributes. The model contributes to 0.8361 of R^2 or -34.70 db of SN ratios η in general estimation. It means the correlation is high and the distribution is closer to the green line. The equation of the line is shown in equation (34).

$$y = 0.6506x \tag{34}$$

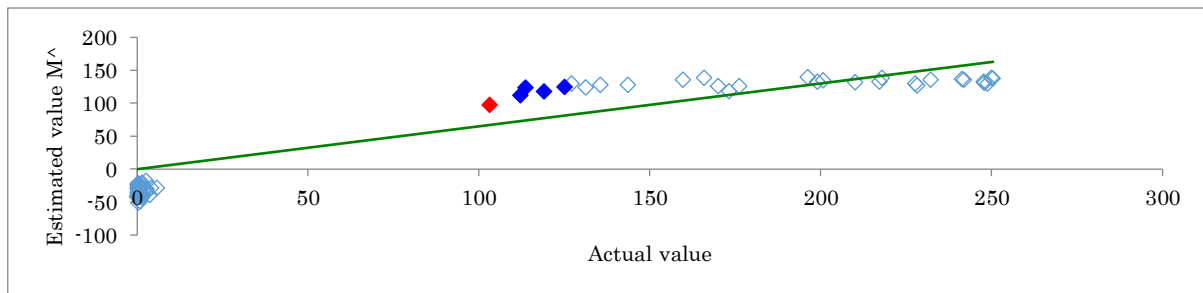


Figure 7. Distribution of actual and estimated signal data values of FBC.

Nevertheless, some of those parameters are useful for integrated estimation, while others are not. Hence, parameters assessment is performed by utilizing L_{64} of OA with level 1 indicates the parameter will be utilized and level 2 indicates the parameter will not be utilized. The value -34.70 db of integrated estimate SN ratio η refers to the first run in L_{64} . Subsequently, the degree of contribution is translated into a bar graph as shown in **Figure 8**. From that, it shows how the parameters are significant to the output. When the parameter 34 which represents fasting blood sugar has been used (level 1) with a greater relationship (SN ratio = -34.44 db) to the output and when the parameter has not been used (level 2) with a smaller relationship (SN ratio = -35.13 db) to the output, the parameter would obtain a higher degree of contribution (0.68 db) which is a positive contribution to the output. On the other hand, when the parameter 6 which represents mean corpuscular haemoglobin (MCH) has been used (level 1) with a smaller relationship (SN ratio = -34.84 db) to the output and when the parameter has not been used (level 2) with a greater relationship (SN ratio = -34.73 db) to the output, the parameter would obtain a lower degree of contribution (-0.12 db) which is a negative contribution to the output.

Positive degree of contribution means that the use of parameter produces the effect of elevating the output of MD whereas negative degree of contribution means that the use of parameter produces the effect of lowering the output of MD. Consequently, parameter 1, 5, 8, 16, 22, 26, 27, 29, 30, and 34 are positive degree of contribution whereas parameter 2, 3, 4, 6, 7, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 20, 21, 23, 24, 25, 28, 31, 32, and 33 are negative degree of contribution. This research work is suggested that in order to obtain lower MD, positive degree of contribution should be decreased while negative degree of contribution should be increased.

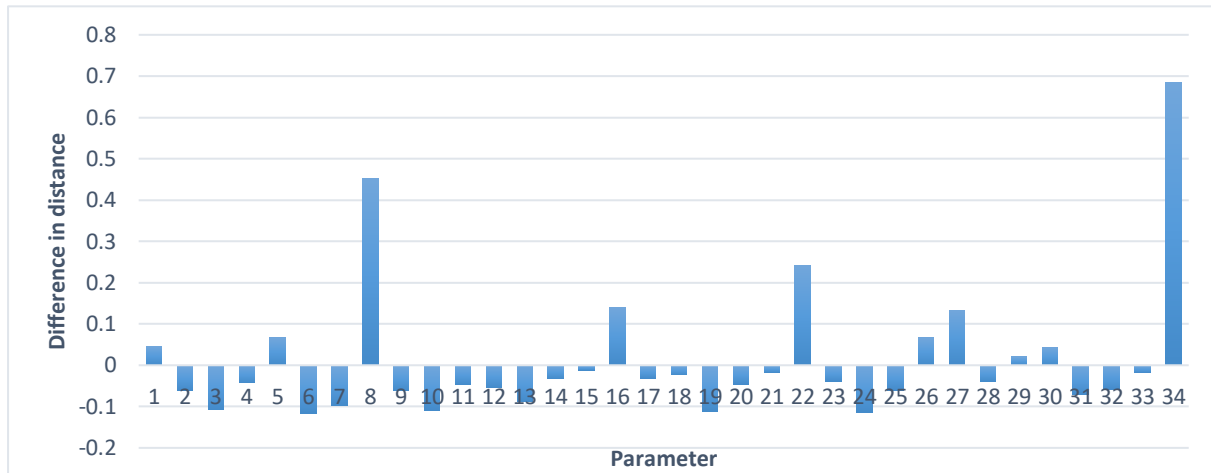


Figure 8. Degree of contribution of FBC.

The purpose of diagnosis of unknown data is to measure the MD and evaluate their parameters for each sample. The normalization is performed by subtracting from the average value of the parameters in the healthy group. The results of estimated value \hat{M} or MD for unknown data are calculated through the equation (26) and subsequently, can be seen in Table 5.

Table 5. The estimated value \hat{M} (MD) for unknown data in FBC

No. of sample	Estimated value \hat{M} (MD)
1	-61.5241
2	-21.1631
3	-19.5001
4	-22.4527
5	-18.7033
6	82.5352
7	110.9596
8	120.5210
9	121.9595
10	118.0532
11	48.1480
12	46.5047
13	46.1079
14	45.2736
15	47.8133

Figure 9 shows a scatter diagram of the estimated values after subjected to the ecosystem which has been developed during optimization of FBC blood tests. The x-axis represents the actual values of the output, M and the y-axis represents the estimated values of the output, \hat{M} . Since the actual values are unknown, the positions of unknown data on the x-axis use the same values as the estimated values. The position of 15 samples of unknown data are marked as green triangle in Figure 8. It can be concluded that 5 unknown samples are closely belong to the healthy group, 5 unknown samples are belonging to the unhealthy group, and another 5 unknown samples are belonging to the outlier.

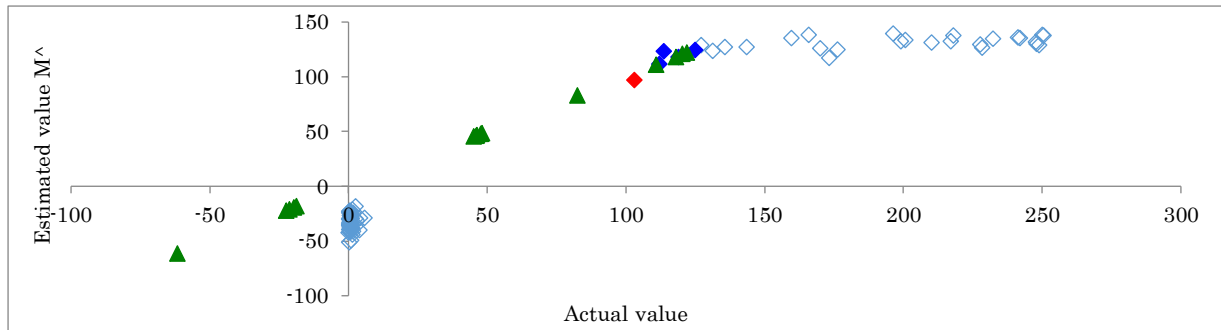


Figure 9. Interpretation of unknown data in FBC.

Figure 10 shows the degree of contribution in the first sample of unknown data in FBC. Consequently, parameter 1, 3, 4, 8, 12, 14, 15, 16, 17, 18, 23, 24, 29, 33, and 34 are positive degree of contribution whereas parameter 2, 5, 6, 7, 9, 10, 11, 13, 19, 20, 21, 22, 25, 26, 27, 28, 30, 31, and 32 are negative degree of contribution. This research work is suggested that in order to obtain lower MD, positive degree of contribution should be decreased while negative degree of contribution should be increased.

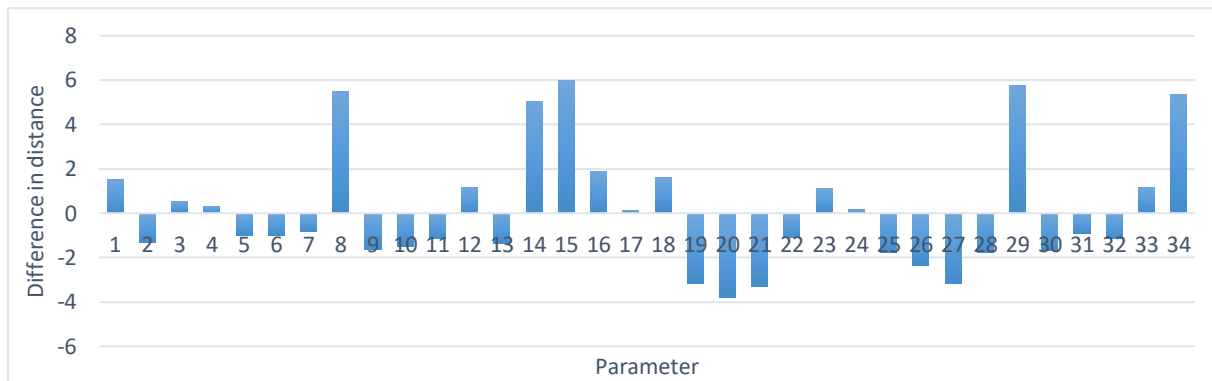


Figure 10. Degree of contribution in first sample of unknown data in FBC.

There are two types of degree of contribution. First is the positive degree of contribution indicating that the use of this parameter produces the effect of elevating the output. It means by increasing the value of this parameter, the MD value will be increased as well. Second is the negative degree of contribution indicates that the use of this parameter produces the effect of lowering the output. It means by decreasing the value of this parameter, the MD value will be decreased as well. The purpose of this section is to prove that the purpose solution to the Bandar Pekan clinic which is lowering degree of contribution is the best solution. Thus, this research work has selected blood tests (FBC) sample 1 as a subject matter as shown in Figure 9. The original output for sample 1 FBC is -61.52 as shown in Table 6. The value is compared with 6 types of modification.

Table 6. Comparison between original and types of modification

Original	MD	Modification	MD
1	-61.52	Type 1	-76.08
		Type 2	-19.76
		Type 3	-277.75
		Type 4	-271.07
		Type 5	-43.80
		Type 6	-93.80

The MD value for type 1 modification is -76.08 which is smaller than the original sample. This modification means the higher positive degree of contribution is added with two points (parameter 8, 14, 15, 29, and 34) while lower positive degree of contribution is added with one point (parameter 1, 3, 4, 12, 16, 17, 18, 23, 24, and 33). On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 19, 20, 21, 26, and 27) while the lower negative degree of contribution is subtracted with one point (parameter 2, 5, 6, 7, 9, 10, 11, 13, 22, 25, 28, 30, 31, and 32). Consequently, this modification as proposed solution has been rejected.

The MD value for type 2 modification is -19.76 which is higher than original sample. This modification means the higher positive degree of contribution is subtracted with two points (parameter 8, 14, 15, 29, and 34) while lower positive degree of contribution is subtracted with one point (parameter 1, 3, 4, 12, 16, 17, 18, 23, 24, and 33). On the other hand, the higher negative degree of contribution is added with two points (parameter 19, 20, 21, 26, and 27) while the lower negative degree of contribution is added with one point (parameter 2, 5, 6, 7, 9, 10, 11, 13, 22, 25, 28, 30, 31, and 32). Consequently, this modification as proposed solution has been accepted.

The MD value for type 3 modification is -277.75 which is smaller than original sample. This modification means the higher positive degree of contribution is added with two points (parameter 8, 14, 15, 29, and 34) while lower positive degree of contribution is added with one point (parameter 1, 3, 4, 12, 16, 17, 18, 23, 24, and 33). On the other hand, the higher and lower negative degree of contribution is set as 0. Consequently, this modification as proposed solution has been rejected.

The MD value for type 4 modification is -271.07 which is smaller than original sample. This modification means the higher and lower positive degree of contribution is set as 0. On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 19, 20, 21, 26, and 27) while the lower negative degree of contribution is subtracted with one point (parameter 2, 5, 6, 7, 9, 10, 11, 13, 22, 25, 28, 30, 31, and 32). Consequently, this modification as proposed solution has been rejected.

The MD value for type 5 modification is -43.80 which is higher than original sample. This modification means the higher positive degree of contribution is added with two points (parameter 8, 14, 15, 29, and 34) while lower positive degree of contribution is added with one point (parameter 1, 3, 4, 12, 16, 17, 18, 23, 24, and 33). On the other hand, the higher and lower negative degree of contribution is maintained their value. Consequently, this modification as proposed solution has been rejected.

The MD value for type 6 modification is -93.80 which is smaller than original sample. This modification means the higher and lower positive degree of contribution is maintained their value. On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 19, 20, 21, 26, and 27) while the lower negative degree of contribution is subtracted with one point (parameter 2, 5, 6, 7, 9, 10, 11, 13, 22, 25, 28, 30, 31, and 32). Consequently, this modification as proposed solution has been rejected.

Therefore, the best solution to the Bandar Pekan clinic is modification type 2 because it shows the highest MD value than others which is nearest to the positive value. However, the proposed solution also might be influenced to the total number of positive and negative degree of contribution, and the total number of higher and lower degree of contribution. Also, the proposed solution might be different to the real practice. The interview session with the pharmacist at Bandar Pekan clinic is done to ask her opinions about the classification and optimization using MTS in MFlex program. The question was asked as follow:

Question: How effective is the methadone program that has been conducted since 2005 in addressing patient problems? Only one subject? One pharmacist only?

Answer: In KKBP it is very effective although some patients are not following the rules. This program is to aim harm reduction to the patients. For instance, if the patient taking illegal drugs in his/her daily life, it will lead to HIV. HIV is easily transmitted to one another, for example to his/her own partner. If more and more people are infected with HIV, then they need to be treated. The cost for HIV treatment is even higher than for patients addicted to methadone. So, when a patient is not involved with illegal drugs, they can live their lives as usual even if he addicted to methadone for a long period of time.

Conclusion

From this research, MTS can classify between the healthy and unhealthy data. Besides, it can identify the significant parameters for the FBC in the blood tests. In other words, it is proved that MTS can analyse the significant factors in the blood tests of the MFlex program. In FBC, the average MD of healthy is 1.00 and unhealthy is 187.06. The positive degree of contribution is parameter 1, 5, 8, 16, 22, 26, 27, 29, 30, and 34 whereas the negative degree of contribution is parameter 2, 3, 4, 6, 7, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 20, 21, 23, 24, 25, 28, 31, 32, and 33. 15 unknown samples in FBC blood tests of MFlex program have been diagnosed using MTS. All of them have different number of positive and negative degree of contribution to achieve lower MD. There are 6 types of modification to prove the proposed solution and type 2 modification has been selected as the best solution. A pharmacist from Bandar Pekan clinic has admitted that MTS is able to solve a problem in classification and optimization in the MFlex program. It might be interesting if MTS is applied more in the healthcare sector. The MTS will be more interesting to be applied to the pandemic that hit Malaysia nowadays which is the cases of Coronavirus (Covid-19) where it can be classifying the severe patients of Covid-19, the deaths in a month, and the infection stage.

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