JOURNAL OF MODERN MANUFACTURING SYSTEMS AND TECHNOLOGY (JMMST)
e-ISSN: 2636-9575
VOL. 4, ISSUE 1, 117 – 128
DOI: https://doi.org/10.15282/jmmst.v4i1.7034

ORIGINAL ARTICLE

Application of Mahalanobis-Taguchi system in ascending case of methadone flexi dispensing (MFlex) program

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ABSTRACT – Patient under methadone flexi dispensing (MFlex) program is subjected to do methadone dosage trends like ascending case since no parameters have been used to identify the patient who has potential rate of recovery. Consequently, the existing system does not have a stable ecosystem towards classification and optimization due to inaccurate measurement methods and lack of justification of significant parameters which will influence the accuracy of diagnosis. The objective is to apply Mahalanobis-Taguchi system (MTS) in the MFlex program as it has never been done in previous studies. The data is collected at Bandar Pekan clinic with 16 parameters. Two types of MTS methods are used like RT-Method and T-Method for classification and optimization respectively. As a result, RT-Method is able to classify the average Mahalanobis distance (MD) of healthy and unhealthy with 1.0000 and 21387.1249 respectively. Moreover, T-Method is able to evaluate the significant parameters with 10 parameters of positive degree of contribution. 6 unknown samples have been diagnosed using MTS with different number of positive and negative degree of contribution to achieve lower MD. Type 2 of 6 modifications has been selected as the best proposed solution as it shows the lowest positive MD value. In conclusion, a pharmacist from Bandar Pekan clinic has confirmed that MTS is able to solve a problem in classification and optimization of MFlex program.

ARTICLE HISTORY
Received: 25th November 2021
Revised: 22nd December 2021
Accepted: 23rd December 2021

KEYWORDS
Mahalanobis-Taguchi system
Mahalanobis distance
ascending case
methadone flexi dispensing program
classification
optimization

INTRODUCTION

In 2019, almost 500,000 individuals died as a result of drug use, and drug use disorders resulted in the loss of 18 million years of healthy living, primarily due to opioids. Drug users, especially those who inject drugs, are more likely to suffer from serious and frequently fatal diseases, and many of them are infected with HIV and Hepatitis C [1]. The region of high-income North America has some of the highest rates of cannabis, opiate, and cocaine addiction. Illicit substances have the greatest rates of substance-related mortality with 6.9 deaths per 100 000 people [2].

For more than 30 years, Malaysians have proclaimed drugs to be the nation’s number one adversary, as they are not just a social issue, but also a threat to national security. As a result, Malaysia is dedicated to addressing and combating the drug problem in a comprehensive, integrated, and balanced manner [3]. Drug abuse has a huge impact on society as of the 70% of property crimes are committed while 4% are committing terrorist crimes [4].

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 Tibi. 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 [5].

MTS is used to create reference scales by generating individual scales of measurement for each parameter [6]. Patient under MFlex program in Bandar Pekan clinic is subjected to do methadone dosage trends such as ascending case involving 16 parameters to determine whether the patient has better recovery process or vice versa. In addition, to identify patient with the potential rate to recover, no specific parameters have been used. This proves that the existing system does not have an accurate method of measurement and lack of justification on the recovery rate. Thus, this research work wants to develop a new data monitoring system for the MFlex program using MTS methods as it has never been done in previous studies.

The objective of this research is to analyse the classification and optimization factors in the ascending case, 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.

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LITERATURE REVIEW

In 2019, there were more than 11 million persons who inject drugs throughout the world, with 1.4 million having HIV and 5.6 million having hepatitis C. Nearly 1.2 million people are affected by both. Most of their health risks are because they share infected injection equipment. People who inject or use drugs are 29 times more likely to get HIV than the overall population. Table 1 shows several nations in Europe and North America have been localized HIV epidemics in recent years [1]. In 2018, the number of opioid dependents in the world was skewed by youth ages 19-39 with a percentage of 72.9% with 18,417 drug dependents. The number of opioid dependents identified by youth, teens (13-18 years of age), and adults (40 years of age and older) declined by -2.2%, -20.7%, and -1.6% respectively, relative to 2018 and 2017 [3].

Table 1. Amount of opioid dependents by age in Malaysia, 2013−2018.

Age Category	Age range	2013	2014	2015	2016	2017	2018
Adolescent	13-15	18	28	45	85	72	42
	16-17	168	206	246	301	248	211
	18	219	388	426	440	374	297
Youth	19	460	576	703	854	678	585
	20-24	3,212	3,751	4,986	5,572	4,706	4,435
	25-29	3,968	4,154	4,977	5,719	4,735	4,621
	30-34	4,022	3,961	4,936	5,849	4,820	4,871
	35-39	3,191	3,247	3,976	4,715	3,884	3,905
Adult	40-44	2,261	2,364	2,724	3,130	2,790	2,813
	45-49	1,672	1,512	1,729	1,972	1,680	1,659
	≥50	1,696	1,587	1,920	2,207	1,935	1,828

Since 2005, Malaysia has used the MFlex program of harm reduction to prevent HIV transmission among persons who inject drugs. In Malaysia, drug users are one of the most vulnerable groups to HIV [3]. Methadone is a synthetic agent that works by conquering/filling brain receptor sites affected by heroin and other opiates. Methadone acts to prevent the euphoric and sedation effects of opiates, reduces cravings for opiates which is a major factor for relapse, relieves opiate withdrawal symptoms, allows a person to work and play a role in society normally thus can be taken only once a day due to its slow excretory nature from the body system [5].

Genichi Taguchi has developed the MTS and it is a diagnostic and forecasting tool using multivariate data with no presumption of a statistical distribution [7]. The MTS utilizes the MD as a measuring scale and incorporates the rigorous development of Taguchi to accomplish system diagnosis and dimension optimization. MD was introduced in 1936 by Prasanta Chandra Mahalanobis [8]. MTS is a widely used multisystem pattern recognition tool that has produced successful results in medical diagnosis, early warning, product identification, fault analysis, market administration, and systematic assessment. MTS is also used for the classification and optimization of broad sample data or unbalanced data [9]. The orthogonal arrays (OA) and the signal-to-noise ratios (SNR) are then used to determine the contribution of every parameter and to pick a useful range of parameters [8].

There are two major variations in the distance between the MD and the Euclidian distance (ED) as shown in Figure 1. MD calculates distances in multidimensional spaces, taking into account correlations. In classical techniques, MD is used to find the "nearness" of the unknown point from the middle point of the group(s). Observation is divided into a category from the middle of which the distance is the least. ED also indicates the distance between the "unknown" point and the group mean point, and there are two limitations of the technique: (1) ED does not have a mathematical calculation of how closely the unknown fits the reference range, and (2) it calculates only a proportional distance from the mean point in the group but does not consider the distribution of the points in the group [10].

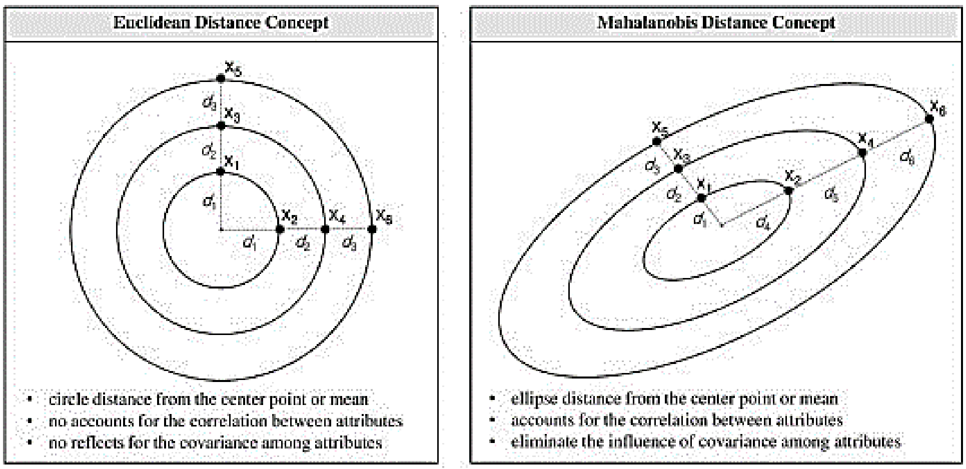


Figure 1. Comparison between MD and ED [11].

The MTS is used to create a continuous scale of measurement and to calculate the abnormality degree [12], it can define critical and non-critical variables [13], and it measures healthy retrospective observations and unhealthy retrospective observations [14]. In contrast, MTS can handle issues with binary classification only [15], characteristic factors may show the covariance matrix and multicollinearity is singular and irreversible which is MD cannot be calculated in this way [16], and it can decide imperative features, but employments the difficult threshold to choose the features [15].

According to Mota-Gutiérrez et al [17], 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 research work has been used these categories to summarize the research gap of the published work from the year 2011 to 2020. In introduction to the method stated the MT method makes it possible to identify anomalies even though learning data is labelled as 'unlabelled' [18]. The standard pattern of MD was introduced for assembled motions to form a standard pattern [19], MD was applied for online tracking and risk detecting [20], and MD quantified the divergence of the candidates' score from the supposedly optimal score [21]. MTS was introduced to tailored the spontaneous fluctuations so as to optimized the subsequent response detection [22].

Abu et al [23] applied MTS to the big-end diameter of connecting rod to distinguish between two distinct ranges within the remanufacturability process spectrum. In 2014, Abu and Jamaludin [24] provided a systematic analysis of the data set on the main journal diameter of crankshaft. Abu et al [25] 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 [26] classified crankshafts' end life into recovery operations based on the Mahalanobis-Taguchi system. Nik Mohd Kamil and Abu [27] 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 [28] identified the critical and non-critical variables during remanufacturing process using MTS and simultaneously estimate the cost using ABC method. Abu et al [29] 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 [30] measured the degree of abnormality using MTS and diagnosed the parameters that influence the system. Nik Mohd Kamil et al [31] 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 [32] identified 4 insignificant and 11 significant parameters in the visual mechanical inspection workstation using MTS. Safeiee and Abu [33] 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 [34] concluded that MTS is a practical method for classification and optimization in the industry. Kamil et al [35] concluded that MTS and TDABC are a great tool and feasible to be implemented in the electronic industry. Saad et al [36] developed MTS based graphical user interface for analysing and classifying the normal and abnormal patient under MFlex service for better monitoring system. Ramlie et al [37] 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 [38] proved that incorporating Bitwise Artificial Bee Colony (BitABC) techniques into Taguchi's T-Method methodology effectively improved its prediction accuracy.

RESEARCH METHODOLOGY

This research work focused on MFlex program under Ministry of Health Malaysia in the methadone dosages. The implementation of the RT-Method and T-Method are using the software MTS provided by Teshima. The 16 parameters of methadone dosage are created into four types of cases which are ascending, descending, up-down, and down-up. Thus, the classification of data and optimization of parameters can be analyzed between those types. To classify whether the patient tend to be healthy or require attention to restore the level of addiction, the methadone dosages contain 16 parameters where it is taken for four years start from 2017 until 2020. Each year are divided into four classes of methadone dosages. Table 2 shows the parameters of methadone dosages with reference range for each classes.

Table 2. Parameters in methadone dosages.

Parameters	Dosage duration	Unit	Reference range
1	Jan-Mar 2017	mg	(160-151)
2	Apr-Jun 2017	mg	(150-141)
3	Jul-Sep 2017	mg	(140-131)
4	Oct-Dec 2017	mg	(130-121)
5	Jan-Mar 2018	mg	(120-111)
6	Apr-Jun 2018	mg	(110-101)
7	Jul-Sep 2018	mg	(100-91)
8	Oct-Dec 2018	mg	(90-81)
9	Jan-Mar 2019	mg	(80-71)
10	Apr-Jun 2019	mg	(70-61)
11	Jul-Sep 2019	mg	(60-51)

12	Oct-Dec 2019	mg	(50-41)
13	Jan-Mar 2020	mg	(40-31)
14	Apr-Jun 2020	mg	(30-21)
15	Jul-Sep 2020	mg	(20-11)
16	Oct-Dec 2020	mg	(10-1)

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 Eq. (1), from *n* number of samples in healthy group.

$$\bar{x}_j = \frac{1}{n}\left(x_{1j} + x_{2j} + \cdots + x_{nj}\right) \ (j = 1, 2, \ldots k) \tag{1}$$

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

$$\text{Sensitivity}, \beta_1 = \frac{L_1}{r} \tag{2}$$

$$\text{Linear equation}, L_1 = \bar{x}_1 x_{11} + \bar{x}_2 x_{12} + \cdots + \bar{x}_k x_{1k} \tag{3}$$

$$\text{Effective divider}, r = \bar{x}_1^2 + \bar{x}_2^2 + \cdots + \bar{x}_k^2 \tag{4}$$

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

$$\text{Total variation}, S_{T1} = x_{11}^2 + x_{12}^2 + \cdots + x_{1k}^2 \tag{5}$$

$$\text{Variation of proportional term}, S_{\beta 1} = \frac{L_1^2}{r} \tag{6}$$

$$\text{Error variation}, S_{e1} = S_{T1} - S_{\beta 1} \tag{7}$$

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

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

$$\text{SN ratio}, \eta_1 = \frac{1}{V_{e1}} \tag{9}$$

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 Eq. (10) and Eq. (11) show the value of Y_1 and Y_2 respectively.

$$Y_{i1} = \beta_i \tag{10}$$

$$Y_{i2} = \frac{1}{\sqrt{\eta_i}} = \sqrt{V_{ei}} \tag{11}$$

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

$$\bar{Y}_1 = \frac{1}{n}\left(Y_{11} + Y_{21} + \cdots + Y_{n1}\right) \tag{12}$$

$$\bar{Y}_2 = \frac{1}{n}\left(Y_{12} + Y_{22} + \cdots + Y_{n2}\right) \tag{13}$$

Finally, MD is calculated through Eq. (14).

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

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 Eq. (3) and Eq. (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 Eq. (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 Eq. (5), Eq. (6), Eq. (7), and Eq. (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 Eq. (10), meanwhile the variable Y_2 is converted first as stated in the Eq. (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 Eq. (12) and Eq. (13) respectively for the prediction of healthy group origin. Lastly, the MD value can be found based on the Eq. (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 Eq. (15) and Eq. (16) respectively.

$$\bar{x}_{\mathrm{j}} = \frac{1}{\mathrm{n}}\left(x_{1j} + x_{2j} + \cdots + x_{nj}\right) \tag{15}$$

$$\bar{\mathrm{y}} = \mathrm{m}_0 = \frac{1}{\mathrm{n}}\left(y_1 + y_2 + \cdots + y_n\right) \tag{16}$$

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 Eq. (17) and Eq. (18) respectively.

$$X_{ij} = \acute{x}_{ij} - \bar{x}_j \tag{17}$$

$$M_i = \acute{y}_i - m_0 \tag{18}$$

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

$$\text{Effective divider}, r = M_1^2 + M_2^2 + \cdots + M_l^2 \tag{19}$$

$$\text{Total variation}, S_{T1} = X_{11}^2 + X_{21}^2 + \cdots X_{l1}^2 \tag{20}$$

$$\text{Variation of proportional term}, S_{\beta 1} = \frac{(M_1X_{11} + M_2X_{21} + \cdots + M_lX_{l1})^2}{r} \tag{21}$$

$$\text{Error variation}, S_{e1} = S_{T1} - S_{\beta 1} \tag{22}$$

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

$$\text{Proportional Coefficint}, \beta_1 = \frac{M_1X_{11} + M_2X_{21} + \cdots + M_lX_{l1}}{r} \tag{24}$$

$$\text{SN ratio}, \eta_1 = \begin{cases} \dfrac{\frac{1}{r}(S_{\beta 1} - V_{el})}{V_{el}} \\ 0 \end{cases} \left(when\ S_{\beta 1} > V_{el}\right)\left(when\ S_{\beta 1} \leq V_{el}\right) \tag{25}$$

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 Eq. (26). Note that, x_{j1}, x_{j2}, …, x_{j6} are the normalized value of each parameter.

$$\text{Integrated estimate value}, \widehat{M}_i = \frac{\eta_1 \times \frac{X_{i1}}{\beta_1} + \eta_2 \times \frac{X_{i2}}{\beta_2} + \ldots + \eta_k \times \frac{X_{i6}}{\beta_6}}{\eta_1 + \eta_2 + \cdots + \eta_6} \tag{26}$$

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

$$\text{Linear equation}, L = M_1\widehat{M}_1 + M_2\widehat{M}_2 + \cdots + M_l\widehat{M}_l \tag{27}$$

$$\text{Effective divider}, r = M_1^2 + M_2^2 + \cdots + M_l^2 \tag{28}$$

$$\text{Total variation}, S_T = \widehat{M}_1^2 + \widehat{M}_2^2 + \cdots + \widehat{M}_l^2 \tag{29}$$

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

$$\text{Error variation}, S_e = S_T - S_\beta \tag{31}$$

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

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

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.

RESULT AND DISCUSSION

The scatter diagram of the methadone dosages between healthy groups and unhealthy groups are created. The samples of healthy and unhealthy groups are computed into two variables of Y_1 and Y_2. The horizontal line represents Y_1 and vertical line represents Y_2. The healthy group (blue dotted) has 50 samples while the unhealthy group (orange dotted) has 9 samples. In addition, the scatter diagrams consist of 16 parameters which have four years start from 2017 until 2020 with 4 classes of months for each of the year. Figure 2 shows a scatter diagram of ascending case 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 0.0212 and the maximum value of MD is 5.7535. Meanwhile, the minimum and maximum value of MD for unhealthy are 17500.0974 and 24748.8462 respectively. This can be concluded that, there is 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 21387.1249. This confirm that both samples are not identical.

The value of correlation coefficient r for healthy samples (blue dotted) is -0.2901. It shows a negative correlation and the relationship between Y_1 and Y_2 variables is only weak. Meanwhile, the correlation coefficient r for unhealthy samples (orange dotted) is 0.3951. Although it is a positive correlation, the relationship between Y_1 and Y_2 variables for the three cases are weak because the nearer the value is to zero, the weaker the relationship.

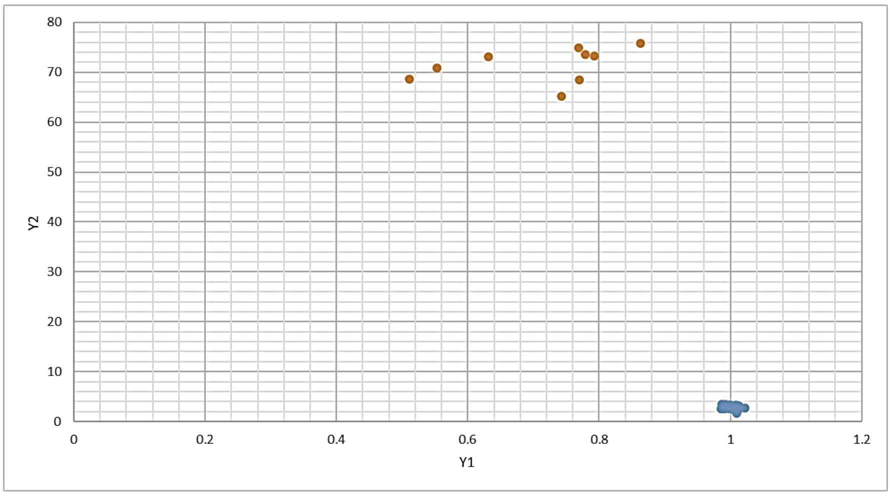


Figure 2. Scatter diagram of ascending case between healthy and unhealthy.

In the ascending case of methadone dosages, the number of healthy and unhealthy samples are 5 and 54 respectively with 16 parameters. The data is organized in the ascending order of output value, as shown in Figure 3. Sample number 4 turns out to be the smallest with 0.021 while sample number 58 turns out to be the largest with 24748.846. This means sample number 49, 6, 1, 30, and 16 are set to be the center point in blue and red dotted.

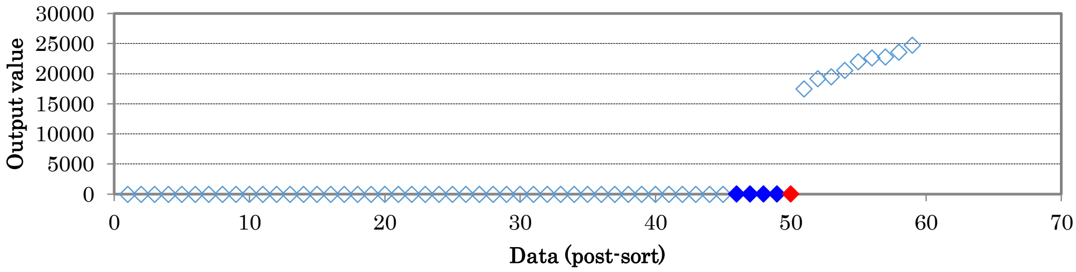
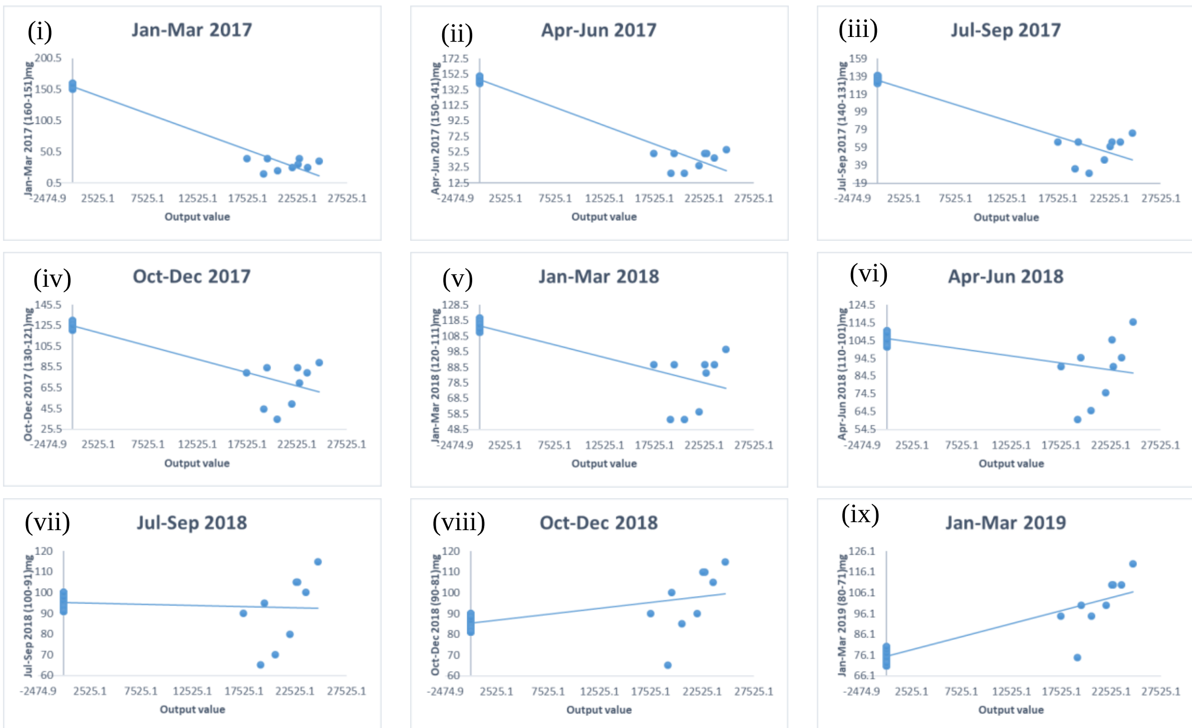


Figure 3. Data (post-sort) for ascending case in methadone dosages.

The relationship between parameters and their output values is shown in Figure 4. 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 [39], 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 4 (vii) which represents the parameter 7 has $5\text{x}10^{-10}$ SN ratio η, so the distribution is far away from a blue line whereas Figure 4 (xiii), Figure 4 (xiv), Figure 4 (xv), and Figure 4 (xvi), which represent the parameter of 13, 14, 15, and 16 has $1\text{x}10^{-6}$ 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 [39] 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 4 (i) until Figure 4 (vii) have negative value of proportional coefficient β whereas the remaining 9 parameters have 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.



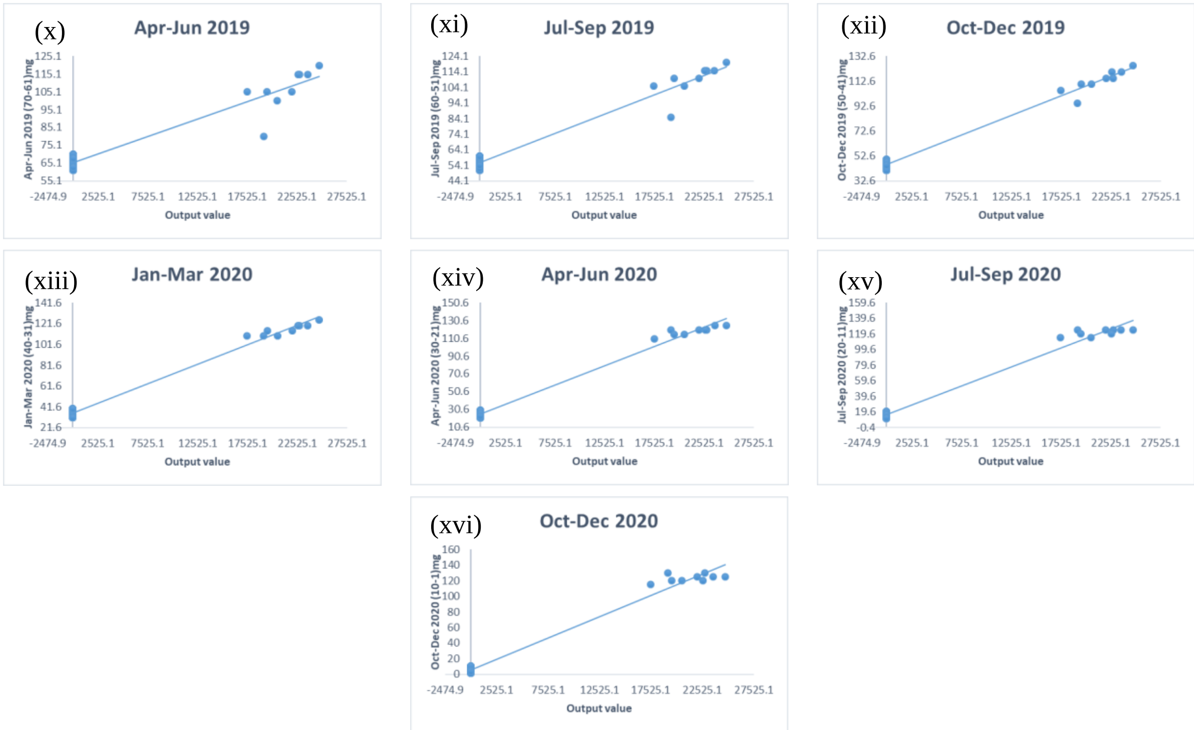


Figure 4. Scatter of normalized output and parameter values of ascending case.

Figure 5 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 0.9944 of R^2 or -55.66 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 Eq. (34).

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

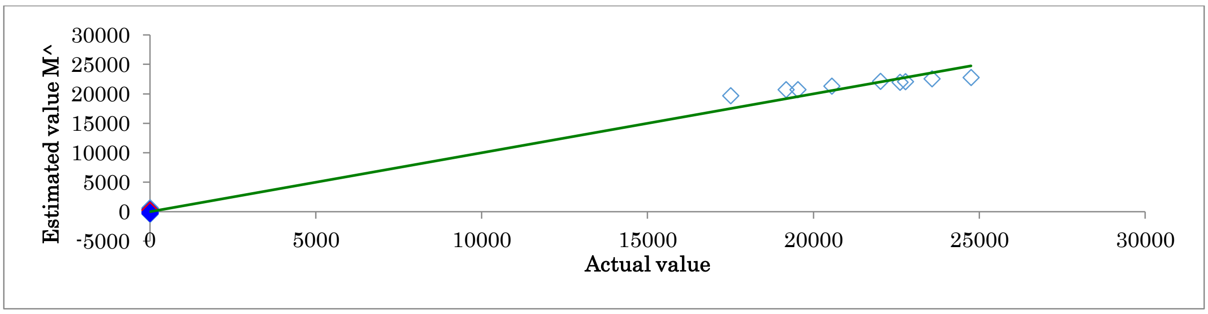


Figure 5. Distribution of actual and estimated signal data values of ascending case.

Nevertheless, some of those parameters are useful for integrated estimation while the remaining are not. Hence, parameters assessment is performed by utilizing L_{20} of orthogonal array with level 1 indicates the parameter will be utilized and level 2 indicates the parameter will not be utilized. The value -55.66 db of integrated estimate SN ratio η refers to the first run in L_{20}. Subsequently, the degree of contribution is translated into a bar graph as shown in Figure 6. From that, it shows how the parameters are significant to the output. When the parameter 13 has been used (level 1) with a greater relationship (SN ratio = -56.17 db) to the output and when the parameter has not been used (level 2) with a smaller relationship (SN ratio = -57.47 db) to the output, the parameter would obtain a higher degree of contribution (1.30 db) which is a positive contribution to the output. On the other hand, when the parameter 2 has been used (level 1) with a smaller relationship (SN ratio = -57.11 db) to the output and when the parameter has not been used (level 2) with a greater relationship (SN ratio = -56.53 db) to the output, the parameter would obtain a lower degree of contribution (-0.58 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 6, 7, 8, 9, 10, 11, 12, 13, 14, and 16 are positive degree of contribution whereas parameter 1, 2, 3, 4, 5, and 15 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.

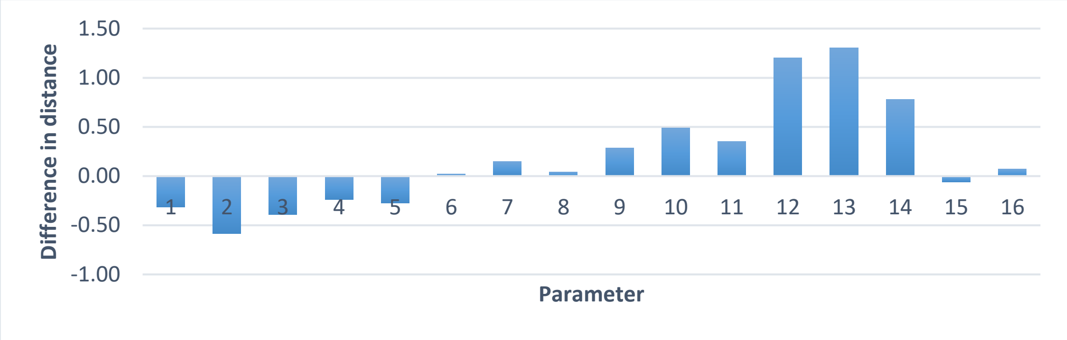


Figure 6. Degree of contribution of ascending case.

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 $M\hat{}$ or MD for unknown data are calculated through the Eq. (26) and can be seen in Table 3.

Table 3. The estimated value $M\hat{}$ (MD) for unknown data in ascending case.

No. of sample	Estimated value $M\hat{}$ (MD)
1	155.1603
2	326.6532
3	20505.3836
4	22609.7097
5	14719.8696
6	5708.0467

Figure 7 shows a scatter diagram of the estimated values after subjected to the ecosystem which has been developed during optimization of ascending case of methadone dosages. The x-axis represents the actual values of the output, M and the y-axis represents the estimated values of the output, $M\hat{}$. 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 6 samples of unknown data are marked as green triangle in Figure 7. It can be concluded that 2 unknown samples are closely belong to the healthy group, 2 unknown samples are belonging to the unhealthy group, and another 2 unknown samples are belonging to the outlier.

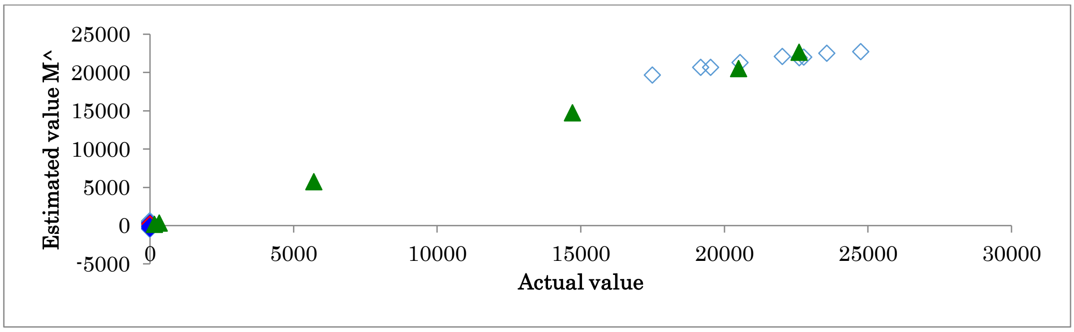


Figure 7. Interpretation of unknown data in ascending case.

Figure 8 shows the degree of contribution in the first sample of unknown data in ascending case. Consequently, parameter 2, 3, 4, 5, 6, 8, 12, 13, and 14 are positive degree of contribution whereas parameter 1, 7, 9, 10, 11, 15, and 16 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.

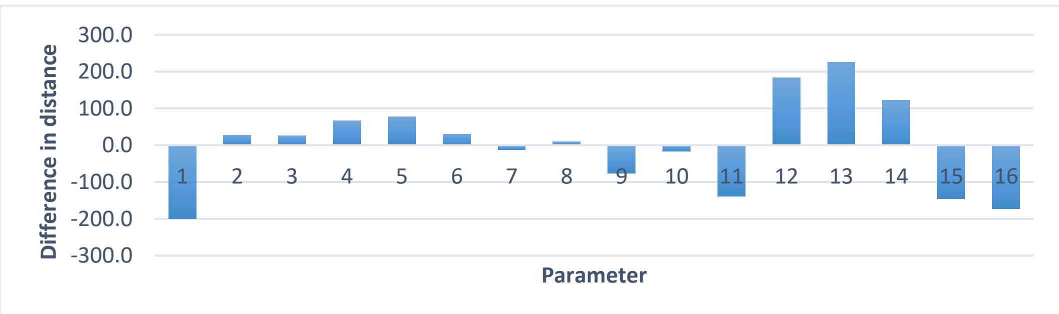


Figure 8. Degree of contribution in first sample of unknown data in ascending case.

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 methadone dosage (ascending case) sample 1 as a subject matter as shown in Figure 13. The original output for sample 1 ascending case is 155.16 as shown in Table 4. The value is compared with 6 types of modification.

Table 4. Comparison between original and types of modification.

Original	MD	Modification	MD
1	155.16	Type 1	268.17
		Type 2	42.15
		Type 3	378.40
		Type 4	-1323.40
		Type 5	374.48
		Type 6	48.85

The MD value for type 1 modification is 268.17 which is larger than the original sample. This modification means the higher positive degree of contribution is added with two points (parameter 4, 5, 12, 13, and 14) while lower positive degree of contribution is added with one point (parameter 2, 3, 6, and 8). On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 1, 9, 11, 15, and 16) while the lower negative degree of contribution is subtracted with one point (parameter 7 and 10). Consequently, this modification as proposed solution has been rejected.

The MD value for type 2 modification is 42.15 which is smaller than original sample. This modification means the higher positive degree of contribution is subtracted with two points (parameter 4, 5, 12, 13, and 14) while lower positive degree of contribution is subtracted with one point (parameter 2, 3, 6, and 8). On the other hand, the higher negative degree of contribution is added with two points (parameter 1, 9, 11, 15, and 16) while the lower negative degree of contribution is added with one point (parameter 7 and 10). Consequently, this modification as proposed solution has been accepted.

The MD value for type 3 modification is 378.40 which is higher than original sample. This modification means the higher positive degree of contribution is added with two points (parameter 4, 5, 12, 13, and 14) while lower positive degree of contribution is added with one point (parameter 2, 3, 6, and 8). 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 -1323.40 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 1, 9, 11, 15, and 16) while the lower negative degree of contribution is subtracted with one point (parameter 7 and 10). Consequently, this modification as proposed solution has been rejected.

The MD value for type 5 modification is 374.48 which is higher than original sample. This modification means the higher positive degree of contribution is added with two points (parameter 4, 5, 12, 13, and 14) while lower positive degree of contribution is added with one point (parameter 2, 3, 6, and 8). 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 48.85 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 1, 9, 11, 15, and 16) while the lower negative degree of contribution is subtracted with one point (parameter 7 and 10). 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 lowest positive MD value compared to others. 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. This research work shows the most important for types of modification is only a suggestion and not practically used in clinic. 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: Based on the degree of contribution graph for the methadone dosages cases, the significant parameters are known when the parameter shows the positive contribution to the output. When the value of output is low for some cases, it does mean the patient is tending to healthy. In your opinion, is this T-Method effective for the use of health authorities to determine the methadone dosage for patients?

Answer: KKBP does not need to know the data of patients either they are healthy or not because it depends on the individual himself to stop this program. Because the aim of this program is not to lower their dose but, to avoid from consume illicit drugs. In addition, this method is beneficial to know how many patients are ascending or decreased their dosages.

CONCLUSION

From this research, MTS is able to classify between the healthy and unhealthy data. Besides, MTS can identify the significant parameters for ascending case in the methadone dosages. In other words, it is proved that MTS can analyse the significant factors in the methadone dosages of the MFlex program. This research work is originally developed four types of cases which are ascending, descending, up-down, and down-up with 16 parameters as stated in Table 2. From the calculation of classification and optimization, the average MD of healthy is 1.0000 and unhealthy is 21387.1249. The positive degree of contribution is parameter 6, 7, 8, 9, 10, 11, 12, 13, 14, and 16 whereas the negative degree of contribution is parameter 1, 2, 3, 4, 5, and 15. There are 6 unknown samples in ascending case methadone dosages 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 confirmed that MTS is able to solve a problem in classification and optimization in the MFlex program. This research work found that it is interesting if MTS is applied more in the healthcare sector, such as 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.

ACKNOWLEDGEMENT

This research was fully supported by PGRS2003154 and the authors fully acknowledge Universiti Malaysia Pahang for the approved fund, and to the Ministry of Health Malaysia for the approval to do research work at Bandar Pekan clinic which makes this research effective.

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