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FACTORIAL EXPERIMENTAL DESIGN AND SIX SIGMA AS TOOLS FOR PROCESS IMROVEMENT IN HEALTHCARE

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Abstract: This paper explores the application of Six Sigma methodology and Design of Experiments (DoE) for improving healthcare processes, using a case study based on data from the Protecal polyclinic. The objective is to demonstrate how statistical and data-driven approaches can enhance process efficiency, reduce variability, and optimize patient outcomes. The research follows the DMAIC (Define, Measure, Analyze, Improve, Control) framework to structure the improvement process. Within this framework, a full factorial experimental design (2^3) is applied to analyze the effects of three key health indicators: ALT, total cholesterol, and glucose on patient body weight. Eight experimental combinations with replications are used to evaluate both main and interaction effects. Regression analysis is employed to model the relationship between input variables and the response, enabling identification of the most significant factors influencing outcomes. The results show that the combined use of Six Sigma and DoE provides an efficient and systematic approach to healthcare optimization, minimizing experimental effort while maximizing information. The study confirms the potential of integrating industrial engineering methods into healthcare systems to support evidence-based decision making and improve overall quality of care.

Keywords: Six Sigma, Design of Experiments, DMAIC, Healthcare Optimization, Factorial Design

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1. INTRODUCTION

In recent decades, the increasing complexity of systems across various industries has created a strong demand for structured, data-driven methodologies aimed at improving efficiency, quality, and performance. Healthcare systems, in particular, are facing significant challenges, including rising operational costs, increased patient expectations, and the need for improved quality of care. These challenges require the implementation of systematic approaches that support continuous improvement and evidence-based decision-making.

One of the most widely recognized methodologies for process improvement is Six Sigma, a data-driven approach originally developed by Motorola in the 1980s. Six Sigma focuses on reducing process variability, eliminating defects, and improving overall performance through statistical analysis and structured problem-solving techniques (Hung & Sung, 2011; American Society for Quality, n.d.; Antony, 2006). The core framework of Six Sigma, known as DMAIC (Define, Measure, Analyze, Improve, Control**)**, provides a disciplined roadmap for identifying problems, analyzing root causes, implementing improvements, and maintaining long-term process stability (Kochov et al. 2016; Srebrenkoska et al., 2016; de Mast & Lokkerbol, 2012).

Numerous studies have demonstrated the effectiveness of Six Sigma across different sectors. For example, its application in manufacturing and food processing industries has led to significant reductions in defect rates and improvements in process efficiency (Hung & Sung, 2011;). Similarly, industrial case studies have shown that Six Sigma can be successfully used to optimize production processes by identifying critical factors and minimizing variability (Srebrenkoska et al., 2016). These results highlight the potential of Six Sigma as a powerful methodology for improving both product quality and operational performance.

Complementary to Six Sigma, the Design of Experiments (DoE) is a statistical methodology used to systematically investigate the relationship between multiple input variables and output responses. DoE enables simultaneous variation of several factors, allowing for the identification of both main effects and interaction effects. Compared to traditional one factor at a time approaches, DoE is significantly more efficient and provides deeper insights into system behavior (Glistau & Coello Machado, 2010; Sokovic et al., 2010).

The importance of DoE lies in its ability to reduce the number of experiments required while maximizing the amount of information obtained. By applying factorial designs and regression modeling, researchers can develop mathematical models that describe the behavior of complex systems and identify optimal conditions for performance improvement (Taguchi, 1986; Montgomery, 2017). Furthermore, DoE allows for the detection of interactions between variables, which are often overlooked in traditional experimental approaches but can have a significant impact on system outcomes (Glistau & Coello Machado, 2010).

The integration of Six Sigma and DoE represents a robust framework for process optimization. Within the DMAIC methodology, DoE is particularly valuable during the Analyze and Improve phases, where it is used to identify key factors, quantify their effects, and determine optimal process settings. This integrated approach has been widely applied in industrial engineering, particularly in manufacturing and logistics systems, where it has resulted in improved efficiency, reduced variability, and cost savings (Glistau & Coello Machado, 2010; Srebrenkoska et al., 2016).

Recent studies have also shown successful applications of Six Sigma in healthcare systems, particularly in reducing waiting times and improving service quality (Gijo & Antony, 2013). Healthcare processes, similar to industrial systems, involve multiple interacting variables that influence outcomes. However, the application of Six Sigma and DoE in healthcare remains relatively limited, especially in clinical and nutritional studies. The adoption of these methodologies in healthcare has the potential to improve patient outcomes, enhance process efficiency, and support data-driven decision-making.

This paper focuses on the application of Six Sigma and Design of Experiments in healthcare, using a case study based on data from the Protecal polyclinic. The study examines key health indicators: alanine aminotransferase (ALT), total cholesterol, and glucose and their impact on patient body weight. A full factorial experimental design (2^3) is employed to systematically evaluate these factors and their interactions, enabling the development of a predictive model for outcome optimization.

The main objective of this research is to demonstrate how the integration of Six Sigma and DoE can be effectively applied in healthcare settings to improve process performance and support evidence-based decision making. By bridging industrial engineering methodologies with healthcare applications, this study contributes to the advancement of interdisciplinary research and highlights the potential of statistical methods in improving the quality and effectiveness of healthcare systems.

2. EXPERIMENTAL PART

Within the framework of this study, the Six Sigma DMAIC methodology was applied for the analysis and improvement of healthcare-related outcomes based on data obtained from the Protecal polyclinic. The quality characteristics of interest were defined in terms of patient health indicators and body weight changes, which represent the primary response of the investigated system. The experimental investigation was conducted using a Design of Experiments (DoE) approach in order to identify the most significant factors influencing the response and to establish a mathematical model describing the process.

The analyzed data were collected from three patients who followed a controlled nutritional program over a period of six months. During this period, several health parameters were monitored, including alanine aminotransferase (ALT), total cholesterol, glucose levels, body weight, and body mass index (BMI). Among these variables, three key factors were selected for the experimental design due to their significant influence on the response:

- X_1 (factor 1) – ALT (U/L)
- X_2 (factor 2) – Total cholesterol (mol/L)
- X_3 (factor 3) – Glucose (mol/L)

The response variable (Y) was defined as the change in body weight of the patients.

A full factorial experimental design with three factors and two levels (2^3 design) was employed. Each factor was examined at two levels, defined as low (–1) and high (+1), based on the observed ranges of the measured values. In addition, the central values (0 level) were determined as the midpoint of the variation intervals in order to define the experimental domain. This approach is widely used for modeling complex systems and identifying significant factors and interactions (Montgomery, 2017; Myers et al., 2016). The selected factor levels for all three patients are presented in Table 1.

Table 1. Factor levels

Factor	Parameter	Low level (–1)	Central value (0)	High level (+1)
X_1	ALT	10 U/L	27,5 U/L	45 U/L
X_2	Cholesterol	3.0 mol/L	4,25 mol/L	5.5 mol/L
X_3	Glucose	3.3 mol/L	4,45 mol/L	5.6 mol/L

The total number of experimental combinations was determined according to:

$$N = p^k = 2^3 = 8 \tag{1}$$

where k represents the number of factors, p represents the number of levels, and N represents the number of experimental runs.

For each experimental combination, two measurements (replications) were conducted, and the mean value of the response ($\bar{y}$) was calculated. This approach enabled estimation of the experimental variance and improved the reliability and accuracy of the obtained results.

The experimental matrix was constructed by systematically varying all factors simultaneously, allowing for the evaluation of both main effects and interaction effects between variables. The obtained results were then used to develop a first-order regression model with interaction terms**,** expressed in coded variables.

The full factorial experimental design enables mathematical modeling of the investigated process within the defined experimental domain. To ensure that the model adequately represents the entire study region, central (base) values of the factors were selected as reference points. These values were determined as the midpoint of the variation intervals:

- X_1 (ALT): 27.5 U/L
- X_2 (Cholesterol): 4.25 mol/L
- X_3 (Glucose): 4.45 mol/L

These central values define the origin of the coded coordinate system and enable transformation between coded and natural variables, which is essential for practical interpretation of the results.

Based on the experimental data, regression equations were developed for each subject, describing the relationship between the selected factors and the response variable. The adequacy of the obtained models was verified using statistical criteria, confirming that the models can be used for prediction and optimization of healthcare outcomes.

3. RESULTS AND DISCUSSION

The experimental results obtained from the 2^3 factorial design, with two replications for each combination, were analyzed in order to determine the influence of the selected factors on the response variable, i.e. body weight.

For each experimental run, the mean value of the response ($\bar{y}$) and the corresponding variance (S_i^2) were calculated (Tables 2–4 for all three subjects). Based on these values, regression models in coded variables were developed for each subject.

Table 2. Results of the experiments for first patient

N	X_1	X_2	X_3	X_1X_2	X_1X_3	X_2X_3	$X_1X_2X_3$	y_1	y_2	$\bar{y}$ (Mean)	S_i^2 (Variance)
1	+1	+1	+1	+1	+1	+1	+1	104.6	99	101.8	15.68
2	-1	+1	+1	-1	-1	+1	-1	96.5	91.5	94.0	12.50
3	+1	-1	+1	-1	+1	-1	-1	94.6	90	92.3	10.58
4	-1	-1	+1	+1	-1	-1	+1	92.1	87.5	89.8	10.58
5	+1	+1	-1	+1	-1	-1	-1	90.6	87.8	89.2	3.92
6	-1	+1	-1	-1	+1	-1	+1	85.6	88.6	87.1	4.50
7	+1	-1	-1	-1	-1	+1	+1	81.4	77.4	79.4	8.00
8	-1	-1	-1	+1	+1	+1	-1	79.9	76.5	78.2	5.78

Table 3. Results of the experiments for second patient

N	X_1	X_2	X_3	X_1X_2	X_1X_3	X_2X_3	$X_1X_2X_3$	y_1	y_2	$\bar{y}$ (Mean)	S_i^2 (Variance)
1	+1	+1	+1	+1	+1	+1	+1	116	111	113.5	12.5
2	-1	+1	+1	-1	-1	+1	-1	108.5	101.9	105.2	21.78
3	+1	-1	+1	-1	+1	-1	-1	102.2	96	99.1	19.22
4	-1	-1	+1	+1	-1	-1	+1	94.5	90.9	92.7	6.48
5	+1	+1	-1	+1	-1	-1	-1	97.5	93.5	95.5	8.00
6	-1	+1	-1	-1	+1	-1	+1	93	88	90.5	12.5
7	+1	-1	-1	-1	-1	+1	+1	93.8	88	90.9	16.82
8	-1	-1	-1	+1	+1	+1	-1	92	89.8	90.9	2.42

Table 4. Results of the experiments for third patient

N	X_1	X_2	X_3	X_1X_2	X_1X_3	X_2X_3	$X_1X_2X_3$	y_1	y_2	$\bar{y}$ (Mean)	S_i^2 (Variance)
1	+1	+1	+1	+1	+1	+1	+1	90	87.4	88.7	3.38
2	-1	+1	+1	-1	-1	+1	-1	86.5	80.9	83.7	15.68
3	+1	-1	+1	-1	+1	-1	-1	84.8	78	81.4	23.12
4	-1	-1	+1	+1	-1	-1	+1	80	75	77.5	12.50
5	+1	+1	-1	+1	-1	-1	-1	81.9	77.5	79.7	9.68
6	-1	+1	-1	-1	+1	-1	+1	77.2	72	74.6	13.52
7	+1	-1	-1	-1	-1	+1	+1	75	72.8	73.9	2.42
8	-1	-1	-1	+1	+1	+1	-1	75	71.8	73.4	5.12

The obtained regression equations are:

a) for the first patient

$$y = 87{,}8375 + 2{,}3125x_1 + 2{,}9125x_2 + 6{,}6375x_3 + 1{,}3875x_{12} + 0{,}2625x_{13} + 0{,}5125x_{23} - 0{,}0625x_{123} \quad (2)$$

b) for the second patient

$$y = 97{,}2875 + 2{,}4265x_1 + 3{,}8875x_2 + 5{,}3375x_3 + 0{,}8625x_1x_2 + 1{,}2125x_1x_3 + 2{,}8375x_2x_3 - 0{,}3875x_1x_2x_3 \quad (3)$$

c) for the third patient

$$y = 79{,}1125 + 1{,}8125x_1 + 2{,}5625x_2 + 3{,}7125x_3 + 0{,}7125x_1x_2 + 0{,}4125x_1x_3 + 0{,}8125x_2x_3 - 04375x_1x_2x_3 \quad (4)$$

The regression coefficients indicate the relative influence of each factor and their interactions on the response. In the experimental design, the terms x_1x_2, x_1x_3, x_2x_3, and $x_1x_2x_3$ correspond to the interaction effects between the factors**,** which may also influence the response variable, as highlighted in similar factorial analyses. Similar findings regarding the dominance of key variables have been reported in previous studies using factorial experimental design and Six Sigma methodologies (de Mast & Lokkerbol, 2012; Gijo & Antony, 2013).

By analyzing the regression equations, it can be observed that the main positive contribution to the response is given by the third factor (glucose, x_3) for all three patients. This indicates that body weight is directly proportional to glucose levels, and its influence is significantly higher compared to the other factors. The second factor, total cholesterol (x_2), also shows a positive effect on body weight, although its influence is smaller compared to glucose.

In contrast, the first factor, ALT (x_1), has relatively low coefficients in all models, indicating that its effect on the response is minimal within the studied range. The interaction effects between the factors were also analyzed. The interaction between cholesterol and glucose (x_1x_2,) shows a moderate influence on the response, particularly for the second subject. The remaining interaction terms have relatively small or negligible effects. This indicates that, although interaction effects exist, the system is predominantly influenced by the main effects, especially glucose. The consistency of these findings across all three patients confirms the reliability and robustness of the experimental design. This is further summarized in Table 5, where glucose (X_3) is identified as the most significant factor, followed by cholesterol (X_2), while ALT (X_1) is found to be insignificant. Based on this analysis, it can be concluded that the regression models may be simplified by neglecting insignificant factors and higher-order interactions. Therefore, the response function can be approximated primarily as a function of glucose, with a secondary contribution from cholesterol.

Table 5. Summary comparison of factors influence (all patients)

Factor / Effect	Patient 1	Patient 2	Patient 3	Overall Conclusion
X_1 (ALT)	Low	Low	Low	Insignificant
X_2 (Cholesterol)	Medium	Medium	Medium	Moderate effect
X_3 (Glucose)	High	High	High	Most significant
X_2X_3 Interaction	Weak	Moderate	Weak	Present but limited
Other interactions	Negligible	Negligible	Negligible	Can be ignored

The adequacy of the developed models was verified using Fisher's criterion (Table 6). The calculated values of the F-test were compared with the tabulated critical value at a significance level of 95% (F_t = 3.69). Since the calculated values were lower than the critical value ($F_p < F_t$), it can be concluded that the models are statistically adequate and can be used for further analysis and prediction.

Furthermore, the comparison between experimental and calculated values shows small deviations, confirming that the regression equations accurately describe the system behavior. This validates the applicability of the developed models for predicting body weight changes under different combinations of input factors.

Table 6. Model validation using Fisher's criterion (example: patient two)

N	$\bar{y}$(Experimental)	y_p(Calculated)	$(\bar{y} - y_p)$	$(\bar{y} - y_p)^2$
1	113.5	109.351	4.149	17.214
2	105.2	109.351	-4.151	17.231
3	99.1	95.901	3.199	10.234
4	92.7	95.901	-3.201	10.246
5	95.5	93.001	2.499	6.245
6	90.5	93.001	-2.501	6.255
7	90.9	90.901	-0.001	0.000001
8	90.9	90.901	-0.001	0.000001

From a practical point of view, the results indicate that glucose control plays a dominant role in weight management, while cholesterol has a secondary influence and ALT has negligible impact. Additionally, the interaction between glucose and cholesterol suggests that combined increases in these parameters may lead to amplified effects on body weight.

Overall, the application of Design of Experiments (DoE) enabled efficient identification of significant factors while minimizing the number of required experiments. The integration with Six Sigma methodology provided a structured and systematic framework for analysis and optimization. The obtained results confirm that statistical and experimental methods can be successfully applied in healthcare systems to improve outcomes and support data-driven decision making**.**

4. CONCLUSION

Within the framework of this study, the Six Sigma DMAIC methodology was applied for the analysis and improvement of healthcare related outcomes based on data obtained from the Protecal polyclinic. Following the proposed improvement model, a three-factor full factorial experimental design (2^3) was implemented in order to investigate the influence of selected health indicators on body weight.

Based on the experimental results, regression equations were developed for all three patients describing the relationship between ALT, cholesterol, glucose, and the response variable. From the obtained models, it was concluded that glucose (x_3) has the most significant influence on body weight, while cholesterol (x_2) has a moderate effect, and ALT (x_1) shows minimal influence within the defined study domain. The analysis of interaction effects showed that the interaction between cholesterol and glucose has a noticeable but limited impact, while other interaction terms can be considered negligible. This indicates that the system is predominantly governed by the main effects, especially glucose.

It was observed that, when the study domain is properly defined, the factorial experimental design provides a reliable approximation of the response function**.** The adequacy of the developed models was verified using Fisher's criterion, confirming that the regression equations are statistically valid and suitable for prediction and further application.

The results demonstrate that the application of Design of Experiments enables efficient identification of significant factors with a reduced number of experiments, while the integration with Six Sigma methodology ensures a structured and systematic approach to process improvement.

From a practical perspective, the findings emphasize the importance of glucose control in weight management, suggesting that healthcare strategies should prioritize regulation of glucose levels, with consideration of cholesterol as a secondary factor.

Overall, this study confirms that statistical and experimental methods can be successfully applied in healthcare systems, contributing to improved process understanding, optimized outcomes, and enhanced decision-making.

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