Since 1983
EPITHEORESE KLINIKES FARMAKOLOGIAS KAI FARMAKOKINETIKES | 42(Sup1): 75-82 (2024)

Received: 13 March 2024 | **Accepted**: 16 May 2024 | **Published**: 27 December 2024

Open Access | **RESEARCH**

Examine the influence of treatment and age on patients affected by high blood pressure

Maysam Sachit Khudair[1,*] Haidar Alnawab[2] Maha Hasan Sultan[3]

[1]Department of Statistics, College of Administration and Economics, University of Baghdad, Baghdad, Iraq
[2]Department of Accounting, College of Business Administration, Al-Bayan University, Baghdad, Iraq
[3]Department of Business Administration, College of Business Administration, Al-Bayan University, Baghdad, Iraq

***Corresponding author:** Maysam Sachit Khudair, Department of Statistics, College of Administration and Economics, University of Baghdad, Baghdad, Iraq; Tel.: +964-7711039238
E-mail: maysam.s@albayan.edu.iq and maysam.sajit1201a@coadec.uobaghdad.edu.iq

ABSTRACT

Background: Hypertension is a major global health concern that increases the risk of cardiovascular disease. Understanding the impact of age and treatment types on blood pressure control is essential for optimizing therapeutic strategies. *Aim*: This study aims to assess how different treatment types and patient age influence blood pressure control in hypertensive patients. *Methodology*: A binary logistic regression model was employed to analyze data from 48 patients diagnosed with hypertension. The study investigated the impact of two treatment regimens and patient age on the likelihood of achieving optimal blood pressure levels. The statistical significance of the findings was evaluated using chi-square tests and *p*-values. *Results*: The analysis revealed that both treatment type and patient age significantly influenced blood pressure outcomes ($p<0.05$). The odds of maintaining controlled blood pressure were significantly higher for patients receiving a combination therapy compared to monotherapy. Older patients demonstrated a slight decrease in the likelihood of achieving optimal blood pressure control. Treatment selection plays a crucial role in hypertension management, with combination therapy showing superior efficacy. Age also influences treatment response, though to a lesser extent. *Conclusion*: These findings highlight the importance of personalized treatment strategies.

KEYWORDS

high blood pressure, logistic, logistic regression, binary logistic, maximum likelihood

How to cite this article: Khudair M. S., Alnawab H., Sultan M. H.: Examine the influence of treatment and age on patients affected by high blood pressure. *Epitheorese Klin. Farmakol. Farmakokinet.* 42(Sup1): 75-82 (2024).
DOI: 10.61873/AICV7932

Publisher note: PHARMAKON-Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. INTRODUCTION

Blood pressure refers to the force exerted by blood against the walls of blood vessels as it circulates through the body's circulatory system. This pressure is generated by the pumping action of the heart, which contracts to push blood into the arteries, supplying oxygen and nutrients to tissues and organs throughout the body. After each contraction (systole), the heart relaxes (diastole) to refill with blood, ensuring continuous circulation through the arteries, including the aorta [1,2].

Medical statistics indicate that normal human blood pressure is approximately 115/75 mm Hg.

Any significant increase or decrease in this pressure can harm the body and lead to various health problems. Systolic pressure, the force exerted during heart contraction, is always higher than diastolic pressure, which occurs during heart relaxation. Maintaining blood pressure within the normal range is crucial to avoid health issues, as high blood pressure increases the risk of conditions such as heart failure, stroke, or kidney failure. Conversely, low blood pressure can lead to cell damage, particularly in the brain, due to insufficient oxygen and nutrients reaching the tissues.

Hypertension, also known as high blood pressure, is a chronic condition characterized by elevated blood pressure levels. In this condition, the heart is under stress as it pumps blood with greater force, leading to the narrowing of thin arteries due to increased resistance during blood flow [3,4]. Blood pressure can also rise in response to the body's increased demand for blood and nutrients, commonly occurring during exercise. Normal blood pressure fluctuates throughout the day in response to nervous influences, psychological stress, and physical exertion.

Statistical applications play a crucial role in understanding and analyzing this condition by employing appropriate models. The use of modern statistical methods in analyzing categorical data has increased, particularly in medical and social research. The logistic regression model is essential for analyzing data where the response variable (*Y*) is binary (0 or 1). There are two types of logistic regression: binary logistic regression and multiple logistic regression. This study will focus on using a binary logistic regression model to identify the relationship between the response variable and the influencing variables.

The primary objective of this study is to examine the effects of blood pressure treatment and patient age on response variables related to high and low blood pressure in hypertensive patients. This will be achieved by constructing an appropriate model to analyze the data.

Several researchers have focused on studying this model in life statistics. For instance, a study on chronic food insecurity in Nepal [5] identified the highest and lowest exponential values of the coefficient obtained from the binary logistic regression model. Logistic regression has also been presented as an effective method for analyzing the effect of independent variables on binary outcomes by measuring the unique contribution of each variable [6].

Further research has employed binary logistic regression in various fields, such as landslide susceptibility [7] and predicting carbon dioxide emissions [8]. The model has been used to predict social trust with demographic variables from a national sample in the General Social Survey (GSS) [9], and it is widely applied in developing clinical prediction models [10].

Moreover, the overall classification performance between random forests and binary logistic regression has been evaluated, considering different substructures, increased variance, noise in explanatory variables, and an increased number of observations [11]. Additionally, guidelines have been developed for clinicians to create logistic regression-based prediction models to enhance clinical decision-making [12].

In Indonesia, binary logistic regression has been utilized to identify factors influencing health insurance ownership and understand their relationships [13]. The research concluded that including age as the only explanatory variable increased the likelihood of obtaining health insurance. The application of binary logistic regression in dental research has also been explored, including aspects like model fit, goodness-of-fit tests, and model validation [14].

2. METHODOLOGY

The importance of using logistic analysis has increased day after day, as it is concerned with analyzing data with a binary response, in which the response variable is usually binary, as in the case of success the response variable takes the value (1) and in the case of failure (Failure) takes the value (0). The logistic model is employed to illustrate the relationship between the response variable (*y*) and the influencing variables, $x_1, \ldots, x_n$, and this relationship is expressed in the following formula [5]:

$$P(x) = \frac{1}{1 + e^{-a - B_i xi}} \quad \ldots (1)$$

Whereas *a*, B_i are the model parameters to be estimated and *P(x)*, *B*>0 the probability of response, $P(Y)$, influenced by the variables *Xi*, and $-\infty < x_i < \infty$, and the above formula is known as the logistic response function and is characterized by the fact that *P*(x) is defined between (1,0) and that the two parameters (*a*, *B*) are not restricted. There are two types of logistic regression models: the binary-response logistic regression model, and the multiple-response logistic regression model [8].

2.1. Binary logistic regression model

The logistic regression model is recognized as a type of nonlinear regression model that describes the relationship between the response variable (*y*) and the independent influential variables. $(x_1, x_2, x_3, \ldots, x_k)$ is nonlinear. The logistic regression model is built on a basic assumption. It means that the response variable (*y*) can take on two values (1,0), and either Success has a probability Of (p_i) or Failure has a probability of $(1 - p_i)$, so the variable (y_i) is distributed according to the Bernoulli distribution (p_i). That is $y_i \sim Ber(p_i),\ i = 1,2,\ldots,n.$ Therefore, the probability density function is according to the following formula [7]:

$$P_r(Y_i = y_i) = p_i^{y_i}\,(1 - p_i)^{1-y_i} \qquad \ldots (2)$$

Since y_i is a binary dependent variable of response (0,1), p_i is the probability of the response occurring when $y_i = 1$, $1 - p_i$ is the probability of the response not occurring when $y_i = 0$.
The probability of a response in the logistic regression model is represented by the value (1) and is calculated using the following formula [15]:

$$P_r(y = 1|\, \mathrm{x}) = \frac{1}{1 + (\mathrm{e}^{B_0 + \sum_{j=1}^{k} B_j \mathrm{x_{ij}}})^{-1}} \qquad \ldots (3)$$

The probability of responding at the value (0) is as follows:

$$P_r(y = 0|\, x) = \frac{1}{1 + \mathrm{e}^{B_0 + \sum_{j=1}^{k} B_j \mathrm{x_{ij}}}} \qquad \ldots (4)$$

The logistic regression function (probability of response) is expressed by the following formula:

$$p_i = \frac{\mathrm{e}^{B_0 + \sum_{j=1}^{k} B_j \mathrm{x_{ij}}}}{1 + \mathrm{e}^{\beta_0 + \sum_{j=1}^{k} \beta_j \mathrm{x_{ij}}}} \qquad \ldots (5)$$

The estimated logistic regression function is as follows:

$$\hat{p}_i = \frac{\mathrm{e}^{\hat{B}_0 + \sum_{j=1}^{k} \hat{B}_j \mathrm{x_{ij}}}}{1 + \mathrm{e}^{\hat{B}_0 + \sum_{j=1}^{k} \hat{B}_j \mathrm{x_{ij}}}} \qquad \ldots (6)$$

We note from equation (12) the shape of the relationship between the influencing variables (x_{ij}) and the probability of response, p_i cannot be linear, but rather takes a curved shape, that is, in the form of the letter (S).

$$1 - p_i = 1 - \frac{\mathrm{e}^{B_0 + \sum_{j=1}^{k} B_j \mathrm{x_{ij}}}}{1 + \mathrm{e}^{B_0 + \sum_{j=1}^{k} B_j \mathrm{x_{ij}}}} \qquad \ldots (7)$$

Where $B_0, B_1, B_2, \ldots, B_j$ represent unknown parameters to be estimated and x_{ij} are influential variables.

2.2. Maximum likelihood method

This method depends on finding the values of $\hat{B}$, which are estimates of the vector B that bring the function to its maximum limit, and assuming that we have r influential variables $(x_1, x_2, \ldots, x_n)$.

The binomial distribution is characterized by two parameters $(n_i,\ p_i)$, where (*Yi*) denotes the sum of successes in each attempt from (n_i) With (*k*) variables affecting each group of sums, the probability density function for (*Yi*) can be expressed as [16]:

$$P_i(X_i = x_i) = C_{x_i}^{n_i} p_i^{x_i} (1 - p_i)^{n_i - x_i}\ ,\, i = 1,2,\ldots,r\ ;\ x_i = 0,1,\ldots,n_i \qquad \ldots (8)$$

The maximum likelihood function of the joint distribution of the data (*Yi*) can be expressed using the formula:

$$L(P) = \prod_{i=1}^{r} C_{x_i}^{n_i} \left[\frac{p_i}{1 - p_i}\right]^{x_i} (1 - p_i)^{n_i} \qquad \ldots (9)$$

The logarithm of the maximum likelihood function is represented as:

$$LnL(P) = \sum_{i=1}^{r} \left\{ LnC_{x_i}^{n_i} + y_i \acute{X}_i B + n_i Ln\left(\frac{p_i}{1 + \exp\,(\acute{X}_i B)}\right)\right\} \ldots (10)$$

The multivariate explanatory binary logistic regression formula is described by the following formula:

$$P(x) = \frac{e^{B_0 + \sum_{j=1}^{n} B_{ij} x_{ij}}}{1 + e^{B_0 + \sum_{j=1}^{n} B_{ij} x_{ij}}} \qquad \ldots (11)$$

The transformation *P(x),* which represents a binary logistic regression model search, is called logit transformation, and the likelihood function is represented by the formula:

$$f(x) = ln\left[\frac{P_i}{1 - P_i}\right] \qquad \ldots (12)$$

2.3. The data

The data for this research study was gathered from the emergency departments of three hospitals: Medical City Hospital, Al-Kindi Hospital, and Imam Ali Hospital, during the year 2017. The dataset comprises information from a sample of 48 patients who underwent blood pressure measurements, taking into consideration their age (Table 1).

Table 1. Treatment data and age for high blood pressure patients.

No	C1	C2	C3
1	Low	Druge1	60
2	Low	Druge1	32
3	Low	Druge1	25
4	High	Druge1	80
5	Low	Druge1	47
6	Low	Druge1	66
7	High	Druge1	81
8	Low	Druge1	48
9	Low	Druge1	48
10	Low	Druge1	49
11	High	Druge1	50
12	Low	Druge1	56
13	Low	Druge1	75
14	Low	Druge1	61
15	High	Druge1	80
16	High	Druge1	50
17	High	Druge1	37
18	Low	Druge1	41
19	Low	Druge1	40
20	Low	Druge1	54
21	Low	Druge1	50
22	High	Druge1	57
23	High	Druge1	52
24	High	Druge1	54
25	Low	Druge1	45
26	High	Druge1	67
27	Low	Druge1	55
28	Low	Druge1	60
29	Low	Druge1	46
30	Low	Druge1	54
31	High	Druge1	51
32	Low	Druge1	46
33	High	Durge2	55
34	High	Durge2	60
35	High	Durge2	61
36	High	Durge2	50
37	High	Durge2	50
38	High	Durge2	63
39	High	Durge2	63
40	High	Durge2	58
41	High	Durge2	59
42	High	Durge2	69
43	High	Durge2	62
44	High	Durge2	68
45	Low	Durge2	50
46	High	Durge2	59
47	High	Durge2	80
48	High	Durge2	51

Blood pressure measurements were taken both upon admission and an hour after treatment administration. This yielded two binary response variables: one indicating low patient improvement and the other indicating no improvement. The age variable is quantitative, while the treatment variable is qualitative and consists of two types: Furosemide and Angised. Some patients received only Furosemide (coded as durag1), while others received both Furosemide and Angised (coded as durag2). Key variables include:

C1: The response variable indicating the health status of patients with high and low blood pressure (low: patient improved, high: patient did not improve).

C2: The treatment variable, descriptive in nature, indicating the type of treatment administered (durag1: Furosemide, durag2: Furosemide and Angised).

C3: The age variable, a quantitative measure.

3. RESULTS

The binary logistic regression model was employed to examine the effect of treatment and age on blood pressure levels among 48 patients. The response variable was binary, indicating whether patients had low (0) or high (1) blood pressure. The sample included 22 patients with low blood pressure readings and 26 with high blood pressure readings, with the latter being the predominant condition.

Table 2 presents the results of the analysis of variance for the model parameters. The chi-square tests and *p*-values for both the treatment variable (C2) and the age variable (C3) were significant ($p<0.05$), providing strong evidence against the null hypothesis (H_0: $\beta_1=\beta_2=0$ *vs* H_1: $\beta_1\&\beta_2\neq0$). This result supports the alternative hypothesis, indicating that both treatment and age significantly influence the patient's blood pressure condition.

The coefficient of determination (R^2) and the adjusted coefficient of determination (R^2(adj)) reflect the explanatory power of the model. An R^2(adj) value of 31.23% is considered reasonable given the sample size, indicating that the model explains a modest portion of the variability in blood pressure levels. The Akaike Information Criterion (AIC) value of 49.53 suggests that the model is efficient, as lower values indicate better model performance.

In Table 3, the estimated coefficients and their standard errors for the model parameters are provided. The coefficient for the treatment variable indicates that when comparing the first treatment (Furosemide) to the second treatment (Angised & Furosemide), the log-odds of high blood pressure decrease by 3.13, assuming the age variable is constant. Similarly, the coefficient for the age variable indicates a decrease in the log-odds of high blood pressure by 0.0698 for each additional year of age. The Variance Inflation Factor (VIF) for both variables was 1, suggesting no multicollinearity issues.

Table 4 displays the odds ratios and confidence intervals for the model. The odds ratio for the age variable (C3) was 1.0723, indicating a slight effect of age on blood pressure levels. However, the odds ratio for the treatment variable (C2) was 22.8682, indicating a substantial impact of the treatment on reducing high blood pressure.

The regression equations for the probability of having high blood pressure, based on the treatments, are as follows:

Regression Equation

P(High)=exp(Y')/(1+exp(Y'))

C2

Druge1 Y'=-4.486+0.06982 C3

Durge2 Y'=-1.356+0.06982 C3

The estimated equation for the probability of improvement due to the effect of the treatment variable (durge 1& durge2).

Table 5 summarizes the results of the goodness-of-fit tests, including the Deviance test, Pearson test, and Hosmer-Lemeshow test. The p-values for these tests exceeded the significance level of 0.05, indicating that the model fits the data adequately.

Based on Figure 1, it appears that the data follow a normal distribution, exhibit equality of variance, and show independence of residuals.

Table 2. represents the results of deviations and testing.

Source	DF	Adj dev	Adj mean	Chi-square	p-value	R^2	R^2(adj)	AIC
Regression	2	22.679	11.3396	22.68	0.000	34.25%	31.23%	49.53
C3	1	5.136	5.1356	5.14	0.000			
C2	1	13.330	13.3298	13.33	0.000			
Error	45	43.529	0.9673					
Total	47	66.208						

Table 3. Results of the estimated model parameters along with the coefficient of variation.

Term	Coefficient	Standard Error Coefficient	VIF
Constant	4.49	1.94	
C3	-0.0698	0.0341	1.00
C2 $_{\text{Durge1Drug2}}$	-3.13	1.12	1.00

Table 4. Risk rate for the Logit model.

Odds	Ratios for odds ratio	Continuous predictors 95% CI
C3	1.0723	(1.0029,1.1465)
C2 $_{\text{Drug2 Durge1}}$	22.8682	(2.5666,203.7561)

Table 5. Goodness-of-Fit Tests.

Test	DF	Chi-square	p-value
Deviance	45	43.53	0.534
Pearson	45	42.54	0.577
Hosmer-Lemeshow	8	7.11	0.525

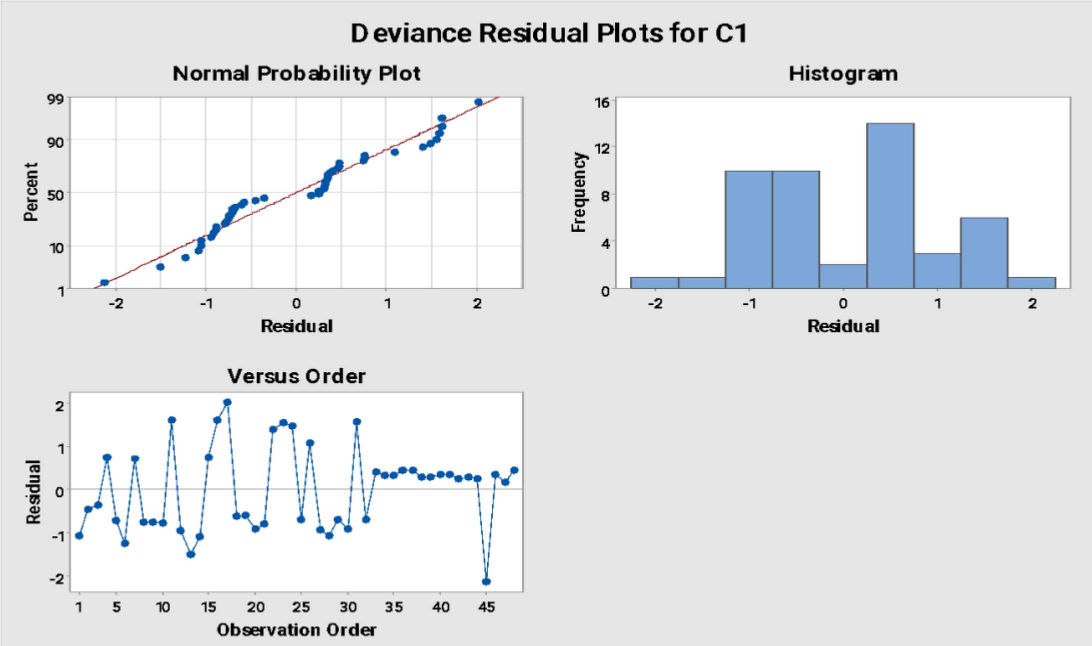

Figure 1. Histogram and the normal probability of model errors.

4. DISCUSSION

The results of this study provide significant insights into the impact of treatment and age on blood pressure outcomes in patients with hypertension. The binary logistic regression model revealed that both treatment type and patient age significantly influence blood pressure levels, with *p*-values well below the 0.05 threshold, indicating strong statistical significance.

The treatment variable demonstrated a particularly profound effect on blood pressure outcomes, with an estimated parameter of -3.13, highlighting a substantial reduction in the odds of high blood pressure when comparing the two treatments (Furosemide and Angised & Furosemide). This suggests that the combination of Angised with Furosemide is more effective in managing blood pressure levels than Furosemide alone. The odds ratio for this treatment was found to be significantly greater than 1, which supports the conclusion that treatment choice plays a crucial role in managing hypertension [17].

In contrast, the age variable, while also statistically significant, showed a more modest effect with an estimated parameter of -0.0698. The odds ratio for age was slightly above 1, indicating that as age increases, the likelihood of lower blood pressure decreases, though the effect is less pronounced than that of the treatment variable. This finding is consistent with existing literature, which often highlights age as a risk factor for hypertension but acknowledges that effective treatment can mitigate some of the age-related risks [18].

When comparing these findings to previous studies, the results align with the broader body of research that underscores the effectiveness of combination drug therapies in managing hypertension. For instance, similar studies have demonstrated that combining multiple drugs often yields better control over blood pressure compared to monotherapy [19]. The current study's findings reinforce the importance of personalized treatment plans that consider both the patient's age and the specific pharmacological intervention.

Moreover, the goodness-of-fit tests, including the Deviance, Pearson, and Hosmer-Lemeshow tests, all indicated that the model fits the data well, with *p*-values exceeding 0.05. This suggests that the logistic regression model used in this study is appropriate for analysing the relationship between the predictors and blood pressure outcomes [20].

In summary, the study's results confirm the critical role of treatment type in managing blood pressure among hypertensive patients, with age also playing a significant but less dominant role. These findings have important clinical implications, suggesting that healthcare providers should prioritize the choice of treatment when addressing hypertension, particularly in older patients. Future research should continue to explore the interaction between different treatments and demographic factors to further refine hypertension management strategies [21].

5. CONCLUSION

This study successfully applied a binary logistic regression model to analyze the impact of treatment type and patient age on blood pressure outcomes. The findings demonstrate that both treatment and age significantly influence blood pressure, with treatment having a more pronounced effect. These results highlight the importance of treatment selection in managing high blood pressure, offering valuable insights for clinical decision-making.

ACKNOWLEDGMENTS

I would like to express my sincere gratitude to Medical City Hospital, Al-Kindi Hospital, and Imam Ali Hospital for assisting me in obtaining the data for this study. I also thank Al-Bayan University for providing the opportunity to share our research at its second conference.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Almobark, K., Nabulsi, A.: Comparing patients with high blood pressure and patients without high blood pressure: types of myocardial infarction and its complications. *Research Square*. 1-10 (2024).
DOI: 10.21203/rs.3.rs-4040130/v1

2. Chen C. H., Liao Y. C., Cheng Y. W., Chung C. P., Lee Y. C., Tang S. C.: High Daily Diastolic Blood Pressure Predicts Incident Stroke, Lacune, and Cerebral Microbleeds in CADASIL. *Journal of Stroke*. 26(1): 112 (2024).
DOI: 10.5853/jos.2023.02880

3. Kim B. S., Yu M. Y., Shin J.: Effect of low sodium and high potassium diet on lowering blood pressure and cardiovascular events. *Clinical Hypertension*. 30(1): 2 (2024).
DOI: 10.1186/s40885-023-00259-0

4. Mishima E.: Constipation and high blood pressure variability. *Hypertension Research*. 47(2): 562-563 (2024).
DOI: 10.1038/s41440-023-01514-5

5. Maharjan K. L., Joshi N. P.: Determinants of household food security in Nepal: A binary logistic regression analysis. *Journal of Mountain Science*. 8: 403-413 (2011).
DOI: 10.1007/s11629-011-2001-2

6. Stoltzfus J. C.: Logistic regression: a brief primer. *Academic emergency medicine*. 18(10): 1099-1104 (2011).
DOI: 10.1111/j.1553-2712.2011.01185.x

7. Pourghasemi H. R., Moradi H. R., Fatemi Aghda S. M.: Landslide susceptibility mapping by binary logistic regression, analytical hierarchy process, and statistical index models and assessment of their performances. *Natural hazards*. 69: 749-779 (2013).
DOI: 10.1007/s11069-013-0728-5

8. Milosavljević B., Pešić R., Dašić P.: Binary logistic regression modeling of idle CO emissions in order to estimate predictors influences in old vehicle park. *Mathematical Problems in Engineering*. 15:1-10 (2015).
DOI: 10.1155/2015/463158

9. Adwere-Boamah, J., Hufstedler S.: Predicting social trust with binary logistic regression. *Research in Higher Education Journal*. 27 (2015).
DOI: 10.18848/1835-2030

10. van Smeden M., Moons K. G., de Groot J. A., Collins G. S., Altman D. G., Eijkemans M. J., Reitsma J. B.: Sample size for binary logistic prediction models: beyond events per variable criteria. *Statistical methods in medical research.* 28(8): 2455-2474 (2019).
DOI: 10.1177/0962280218784726

11. Kirasich K., Smith T., Sadler B.: Random forest vs logistic regression: binary classification for heterogeneous datasets. *SMU Data Science Review*. 1(3): 9 (2018).

12. Shipe M. E., Deppen S. A., Farjah F., Grogan E. L.: Developing prediction models for clinical use using logistic regression: an overview. *Journal of thoracic disease*. 11(Suppl 4), S574 (2019).
DOI: 10.21037/jtd.2019.01.25

13. Astari D. W.: Analysis of Factors Affecting the Health Insurance Ownership with Binary Logistic Regression Model. *Journal of Physics: Conference Series*. 1320 (1): 012011 (2019).
DOI: 10.1088/1742-6596/1320/1/012011

14. Srimaneekarn N., Hayter A., Liu W., Tantipoj C.: Binary response analysis using logistic regression in dentistry. *International Journal of Dentistry*. (2022).
DOI: 10.1155/2022/5358602

15. Shrestha N.: Application of binary logistic regression model to assess the likelihood of overweight. *Am J Theor Appl Stat*. 8(1): 18-25 (2019).
DOI: 10.11648/j.ajtas.20190801.13

16. Fowlkes E. B.: Some diagnostics for binary logistic regression via smoothing. *Biometrika*. 74(3): 503-515 (1987).
DOI: 10.1093/biomet/74.3.503

17. Wright J. T., Williamson J. D., Whelton P.K., *et al*. A Randomized Trial of Intensive versus Standard Blood-

Pressure Control. *New England Journal of Medicine*. 373 (22): 2103-2116 (2015).
DOI: 10.1056/NEJMoa1511939

18. Franklin S. S., Larson M.G., Khan S. A., *et al*.: Does the Relation of Blood Pressure to Coronary Heart Disease Risk Change with Aging? *The Framingham Heart Study. Circulation.* 103(9): 1245-1249 (2001).
DOI: 10.1161/01.CIR.103.9.1245

19. Jamerson K., Weber M.A., Bakris G. L., *et al*.: Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients. *The New England Journal of Medicine.* 359(23): 2417-2428 (2008).
DOI: 10.1056/NEJMoa0806182

20. Hosmer D. W., Lemeshow S.: Applied Logistic Regression. 2nd Edition. *Wiley-Interscience*, (2000).
DOI: 10.1002/0471722146

21. Messerli F. H., Bangalore S., Bavishi C., Rimoldi S.F.: Angiotensin-converting enzyme inhibitors in hypertension: To use or not to use? *Journal of the American College of Cardiology*. 71(13): 1474-1482 (2018).
DOI: 10.1016/j.jacc.2018.01.058