# **International Journal on Robotics**, **Automation and Sciences**

## Chronic Kidney Disease Risk Estimation Using Artificial **Neural Network**

Al-Amoodi Wody, Eko Supriyanto\*, and Muhammad Naqiuddin Mohd Warid

Abstract — Chronic kidney disease (CKD) is the most common disease of the urinary system that can threaten the survival of the human body. Early detection and lifestyle changes can prevent kidney failure and improve the chance of survival. In West Malaysia, the prevalence of chronic kidney disease is estimated to be 9% of the population. However, screening for chronic kidney disease is still neglected at the early stages. Many equations for risk estimation of kidney failure have been developed. Some of the limitations of these equations are that they may require many laboratory tests, static and not updated. In this study, a new risk estimation model for kidney disease is developed. The risk factors of kidney disease are first identified according to their energy levels, which are Low, Medium and High. The new equation is then developed based on the relationship and the estimated weight of these risk factors. Artificial Neural Network (ANN) is utilized in this study as an alternative to classic risk equations. The MATLAB software is used to train the neural network. Retrospective data from 20 subjects are used to compare the output for the conventional equation and ANN. Another 20 samples have also been generated and compared with "Kidney Disease: Improving Global Outcomes" (KDIGO) 2012 clinical guideline heat map. The results show a slight difference between the methods. The conventional method shows its capability to estimate the risk. The result also shows the potential of the artificial neural network (ANN) to improve the accuracy of chronic kidney disease risk estimation.

#### Keywords—Risk Estimation, Artificial Neural Network.

#### Ι. INTRODUCTION

Chronic kidney disease (CKD) is caused by the failure of kidney to filter out the blood from waste materials, according to National Chronic Kidney Disease [1]. The main causes of CKD are the damage and injuries of the nephrons that responsible for urine filtration. The nephrons can be damaged by many acute diseases gradually with time. Signs of CKD may include weakness, shortness of breath, numbness, muscle cramps and loss of appetite [10]. In the United States, 30 million people (15% of the adult) are estimated to have CKD. In Malaysia, kidney diseases considered as one of the top ten diseases that cause a high number of fatalities. This indicates that kidney disease is still one of the most aggressive diseases that needed to be prevented. Many changes can lead to a reduction of this disease such as drinking more fluid, diabetes treatments, changes in diet, reduce the cholesterol level and physical activity [9]. Risk factors of CKD include diabetes and hypertension, which can lead to a total loss of filtration and kidney failure. Other factors such as race, age, and gender, play a major role in determining the Glomerular Filtration Rate (GFR). Creatinine serum and Creatinine to Albumin (ACR) levels can significantly determine the kidney condition and determine the stage of kidney failure. Other related factors such as smoking and drinking water, can improve kidney filtration and reduce the risk of being diagnosed with chronic kidney disease.

Early screening, kidney stage classification and risk estimation of the kidney can help reduce fatality chances and improve survival rate. By estimating the kidney functionality, medication and life changes can be followed to prevent the occurrence of this disease. Therefore, a higher awareness of kidney screening is very vital. Many equations and risk estimations are already being used for risk assessment of kidney failure and stage classification, for example, the Tangri equation (4 variables) [2]. Most of these equations were created by using many variables to detect the kidney condition. The four variables used

Eko Supriyanto is with the Advanced Diagnostics and Progressive Human Care Research Group, IJN-UTM Cardiovascular Engineering Centre and School of Biomedical Engineering and Health Sciences, Faculty of Engineering, Universiti Teknologi Malaysia, 81310 Johor, Malaysia (e-mail: eko@utm.my).



International Journal on Robotics, Automation and Sciences (2019) 1:1-10 https://doi.org/10.33093/ijoras.2019.1.1

Manuscript received: 3 May 2019 | Revised: 10 Sept 2019 | Accepted: 14 Oct 2019 | Published: 13 Nov 2019

© Universiti Telekom Sdn Bhd. Published by MMU PRESS. URL: http://journals.mmupress.com/ijoras This article is licensed under the Creative Commons BY-NC-ND 4.0 International License



<sup>\*</sup>Corresponding author. Email : <u>eko@utm.my</u> ORCID: 0000-0002-6766-793X Al-Amoodi Wody and Muhammad Naqiuddin Mohd Warid are with the School of Biomedical Engineering and Health Sciences, Faculty of Engineering, Universiti Teknologi Malaysia, 81310 Johor, Malaysia. (e-mail: wody.alamoudi@gmail.com).

in the original Tangri equation include age, gender, race, GFR and albumin/creatinine ratio (ACR). However, the GFR is calculated using different equations like CKD-EPI creatinine-based [3], creatinine-cystatin [4], and MDRD equation [5]. The estimations and the results from these equations can be very different for different regions and countries. Creatinine serum test and cystatin C test are required to verify the results.

All these equations can lead to different results between different countries and regions and require certain modification to be applied correctly. These equations, which have been created in the past decade, may not always be updated or fixable. This may lead to lower results and incorrect outcome in the future. Moreover, the main issue of this equation is that they rely on laboratory results like ACR and serum creatinine, to estimate the functionality and the possibility of getting CKD. A new approach is needed to determine an estimation without the need of these laboratory results.

Many studies have been conducted to investigate the use of computational intelligence method in detecting diseases at an early stage by estimating the risk. Examples of the method being studied are fuzzy logic [6,7], expert system [8,9,10] and artificial neural network (ANN) [11,12,13]. These methods have different expertise requirements, data input, and output accuracy.

ANN is an adaptive, self-learning computational technique, mimicking the function of the cerebrum, which depends on an expansive gathering of neural units that connected to numerous other units. It has been used in the medical field for biochemical analysis [14], diagnostic [15], image analysis [16] and drug design [17].

ANN is chosen for this study because it has the ability to learn how to do tasks based on the data given for training and develop its own organization. Multiple neural network computations can be operated in real-time [13]. ANN can be used to facilitate the screening for kidney classification and to improve early detection of kidney failure. The new risk estimation is developed based on energy levels. The risk estimation model also will be developed to be dynamic and can adapt to the future. The equation will include multiple dynamic factors like a database, weighted risk factor, and interpolation.

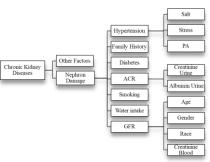
The objective of this study is to develop a new approach to calculate the risk of CKD and using ANN to create a new risk estimation. In this study, two methods will be used to estimate the CKD risk. The first method is a conventional method, where the development of the static equation will be carried out based on the retrospective data that has been gathered from the literature, and the equation will be designed based on the risk factor energy level. The second method, which will be using ANN, recognition of pattern will be utilized to estimate the risk using the conventional method as the core of this design. This design will then have the ability to be improved with time. The expected output of this model is to be able to estimate the risk without relying on laboratory results.

#### II. METHOD AND MATERIALS

Kidney failure can be caused by multiple risk factors. These factors interlinked with each other and indicate the status of the nephrons. Kidney failure is caused by the inability of the kidney to filter out the waste product from the blood, which causes harmful materials to re-enter our body. This may cause by damaged nephrons, the main unit responsible for filtration. This tends to happen as age is increased.

Besides age, the non-modifiable factors are genetics, gender, and race. Since the main cause of kidney failure is kidney damage, it is very important to evaluate kidney function by checking the presence of waste in blood and the presence of protein and blood in the urine. There are other related factors that affect kidney function like protein and blood presence in the urine. Other body systems also involve in kidney diseases, for example, an increase of blood sugar and blood pressure that can lead to kidney failure.

Lifestyle and environment have significant impacts on the body system and bioenergy symphony as shown in Figure 1. These factors could be the amount of fluid or drinks that are consumed, the amount of physical activities and environmental effects to the body system. Public awareness of keeping a healthy lifestyle can greatly reduce the chances of having kidney diseases.



#### FIGURE 1. Block Diagram for Risk Factors of CKD.

From physiology perspective, CKD risk factors can be classified based on three energy levels: low, medium and high energy levels. Low energy level risk factors are related to molecular structure, which is dependent on non-modifiable factors such as age, gender, and race. Incidence of CKD has been found to be directly proportional with age. Medium energy level risk factors are related to body systems, which include the cardiovascular system, digestive system, and urinary system. High energy level risk factors are related to lifestyle activities such as food consumption, physical activities and environmental factors. Table 1 shows the classification of CKD risk factors.

No.	Low Energy Level (LEL): Molecular Structure	Medium Energy Level (MEL): Body System	High Energy Level (HEL): Bioenergy Symphony
1	Gender	Hypertension (H)	Salt (S)

		Energy Level					
No.	Low Energy Level (LEL): Molecular Structure	Medium Energy Level (MEL): Body System	High Energy Level (HEL): Bioenergy Symphony				
2	Race	Albumin to creatinine ratio (ACR)	Water Intake (WI)				
3	Age	Blood Wastes (BW)	Physical Activity (PA)				
4	Family History	Diabetes (D)	Tobacco (T)				
5	-	Glomerular filtration rate (GFR)	Stress (St)				

#### A. Database from Literature

As shown in Table 1, CKD relies on multiple risk factors. Figure 2 shows the result of the National Health and Nutrition Examination Survey 1999-2004 (NHANES), which found that all stages of CKD are more prevalent at older ages [18]. There are variety of conditions that could damage the kidneys, such as diabetes and hypertension, as well as declining kidney function due to unknown reasons. The Baltimore Longitudinal Study of Aging (BLSA) has also found that kidney functions inclined to deteriorate with age [19]. The study has measured and discovers that creatinine clearance reduced on average by 0.75 ml/min/year. Some of these older patients with CKD will advance to End Stage Renal Disease (ESRD). Therefore, it is a major challenge healthcare professionals to identify for this population. In the CREDIT study, a population-based survey in Turkey stated that the odds ratios of CKD ranged from 1.45 to 2.18 for every 10-years increased in age among subjects aged above 30 years old in Turkey [20]. This finding will be applied in the equation developed in this study.

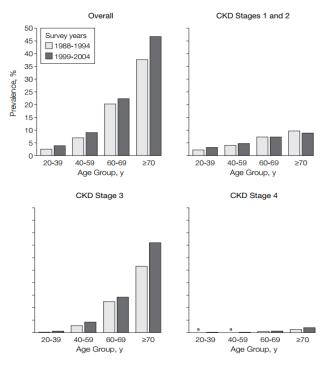


FIGURE 2. Prevalence of Chronic Kidney Disease (CKD) Stages by Age Group (Coresh et al., 2007).

Studies show that gender is one of the main risk factors for CKD [21], and generally, the prevalence is greater in women. Based on the CKD-EPI creatinine equation [22], it shows that female has a higher risk of CKD. An annual data report from US Renal Data System [23] shows that, between the year 2007 and 2012, the incidence of chronic renal failure in women was higher (15.1%) than in men (12.1%). Swedish National Study on Ageing and Care [24] has reported that the percentage of women with CKD was higher than men. In a sample size of 1252 people, the study used cystatin C and creatinine as its method for GFR assessment. While in Switzerland, a cross-sectional study also reported that women have a higher prevalence of CKD [25]. Brown et al. [26] (14.4% in men and 16.2% in women, p = 0.09) and Chadban et al. [27] 9.3% in men and 13.0% in women, p = 0.002) both reported higher prevalence in women.

Similarly, the race is considered as one of the risk factors related to CKD. In a population-based study in the United States, the incidence of CKD was higher among African-American adults, compared with white adults [28]. Figure 3 shows the incidence of CKD according to race and attained age. It shows that African Americans demonstrated a higher risk for every age after 45 years (log-rank test, P 0.001). Muntner et al. also reported the similar findings, where African Americans had a two- to three-fold higher risk of getting CKD compared to white Americans, due to the higher levels of albuminuria [29].

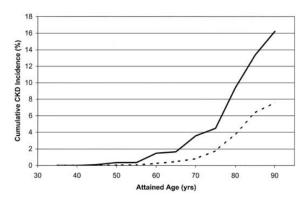


FIGURE 3. Cumulative incidence of chronic kidney disease (CKD), in the Second National Health and Nutrition Examination Survey (NHANES II), 1976 to 1992 [22]. Solid line, African Americans; dashed line, whites.

Chronic kidney disease can also be affected by genetic. Family members of CKD patients have a high prevalence as found by Song et al [30]. The association of CKD with other inherited diseases like diabetes and hypertension may explain some of the familial factors. In another study, McClellan et al. also reported a significantly increased risk for CKD associated with a positive family history (adjusted hazard ratio of 1.93; 95% confidence interval, 1.22-3.07) [31].

Medium Energy Level (MEL) risk factors are related to the human body system, which includes biomarkers, existing medical conditions, and urinary test results. The two major indicators that affect CKD are glomerular filtration rate (GFR) and albumin to creatinine level (ACR). GFR can represent the amount of filtration that has been done in the kidneys. Kidney function and stage can be determined by the GFR factor. During the assessment of chronic kidney disease, GFR can help understand the development of CKD. GFR can be determined by using many equations, based on age, gender, race and serum creatinine of blood. However, the CKD-EPI equation seems to have higher accuracy than other factors [32].

Albumin to Creatinine Ratio level (ACR), an indicator for CKD [33], is obtained by urinary laboratory analysis. Based on the urinary results, it can show how much the damage to the kidney has been done [34]. The presence of albumin in the urine is one of the major signs of a damaged kidney. Creatinine levels in the urine can also determine the filtration quality [35]. Usually, a damaged kidney will result in a lower creatinine level. The ratio of albumin to creatinine level is very crucial in the risk estimation.

Diabetic patients are prone to suffer CKD in their lives. Low production of insulin in diabetic patients will cause a high blood sugar level [36]. This can cause damage to the blood vessel supplying the kidney, which eventually will lead to chronic kidney failure and increase wastes build up in the body.

High blood pressure is one of the leading causes of CKD. It increases the force of blood during circulation [37]. It has been found to occur in 85% to 95% of CKD patients [38]. Conversely, CKD can also cause hypertension. Uncontrolled hypertension can lead to damage to the kidney's vasculature. This will cause a more rapid progression of CKD which then can exacerbate hypertension.

High Energy Level (HEL) risk factors include water intake and tobacco smoking. Salt intake, stress level, and physical activity are HEL risk factors that associated with hypertension. Studies showed that there is a significant effect of water intake to CKD. An antidiuretic hormone or arginine vasopressin (AVP), is essential to the regulated thirst in humans but it has a vasoconstrictive effect. Increased AVP level can have negative effects on renal hemodynamics and blood pressure [39]. Low water intake (less than 2.1L per day) have a higher risk of renal failure and CKD, while increased water intake will suppress the AVP level.

Tobacco smoking is one of the risk factors for CKD too. It can lead to reduced renal function, due to narrowing of the blood vessel and blood flow that supply the kidneys. This has been shown in a study by Yacoub et al. [40] where smoking was found to significantly increase the risk of CKD (Odds Ratio = 1.6, p = 0.009, 95% CI = 1.12-2.29). Figure 4 shows the relationship between smoking and its risk.

Maintaining a healthy range of blood pressure is essential in managing or preventing CKD. One of the factors that can contribute to high blood pressure is high salt (sodium) intake [41]. Studies show that excessive sodium intake can increase blood pressure and lead to fatal diseases. Due to increasing sodium level in the blood, it will reduce the ability of the kidney to filter water outside the body, which results in high blood pressure. A study in Sweden shows that lower stress resilience can relate to hypertension and increase blood pressure [42], due to the release of some hormones during stressful events. These hormones may damage the blood vessel, lead to high blood pressure and subsequently causing the patient to suffer CKD. Therefore, daily repeated stressful events can lead to hypertension, while reducing stressful events can lower the risk of getting many diseases.

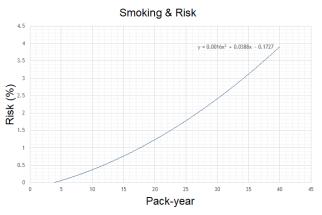


FIGURE 4. Smoking and Risk Relationship.

Physical activity is another factor associated with hypertension and chronic kidney disease preventions [43]. Routine physical activity can improve the blood flow by pumping the blood with minimal work and reduce the force in arteries. This will lower the blood pressure and energize the flow to the kidney and other parts of the body.

#### B. An Algorithm Using the Classic Risk Equation and Neural Network

The conventional equation of chronic kidney disease is based on the relationship between the risk factors as shown in Figure 5. Each factor has been assigned a certain weight based on their relationship.

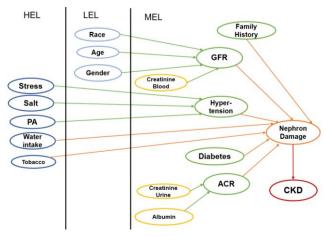


FIGURE 5. Classic Risk Method.

The accuracy of the risk percentage will be higher if more inputs are applied to the equation. Based on the relationship, the equation for the conventional method is formulated:

$$\begin{aligned} Risk (\%) \\ &= \left[ 46\% \left( 0.8 * \left( \frac{age}{10} \right) \right) \\ &+ 5\% (0 \text{ or } 1)(race) \ 3\% \ (0 \text{ or } 1)(gender) \\ &+ 46\% \ \left( \frac{Creatinine \ blood}{10} \right) OR \ GFR \ risk \right] * \ 34\% \\ &+ 4\% \ (water \ intake) + 5\% \ (tobacco \ per \ year) \\ &+ 12\% (hypertension) + 3\% \ (family \ history) \\ &+ \ 8\% \ (diabetes) \\ &+ \left[ 50\% \ \left( \frac{creatinine \ urine}{10} \right) \right) \end{aligned}$$

+ 50% (log (albumin urine)/2.48) OR 100% log  $\left(\frac{ACR}{3}\right)$ 

= 34%

An example of using Microsoft Excel to calculate the risk by the conventional method is shown in Figure 6. The risk is classified based on the percentage range and assigned a specific color.

The conventional method is compared with the artificial neural network (ANN) method. The ANN method is first rained using the conventional equation by using MATLAB. Fed forward pattern recognition method is used to build a network that able to produce a risk percentage based on the data input. The inputs are chronic kidney disease risk factors. The network has been designed with 16 input, 80 hidden layers and 1 output with a total of two layers, namely, hidden and output. The design is shown in Figure 7.

	Kidney Failure Risk Calculator												
Risk Factor	Unit	Value	Notes										
Age	Years	80	Maximum 100										
Gender	Female/Male	YES	1 for Female and 0 for Male										
Race	Black or other	s NO	1 for Black and 0 for Others										
Smoking	Pack-Year	5	per day and years smoking										
Water	L	2.2	Maximum 4.4										
Salt	Gram/Day	3	maximum 25										
Diabetes	Yes/No	NO	Have Diabetes?										
Family History	Yes/No	NO	Family history with CKD										
Phyiscial Activity	Yes/No	YES	YES if Light Physical Activity										
Stress	Yes/No	NO	Stressfull enviornment										
Hypertension	Yes/No	NO	Have Hypertension?										
Creatinine Blood	mg/dL	0.6	Creatinine Serum										
Albumin Urine	mg/24h	20	Urinary Results										
Creatinine Urine	mg/24h	250	Urinary Results										
ACR	mg/g	80	Albumin/Creatinine										
GFR	mL/min/1.73 r	n^2 86.1	Glomerular Filtration Rate										
		Results											
Risk %		39%											
Risk Level	Low												
Risk Color													
Risk	B	isk Range	Risk Color										

Risk	Risk Range	Risk Color
Very low	0-20%	
Low	20-40%	
Medium	40-60%	
High	60-80%	
Very High	80-100%	

FIGURE 6. Conventional Method Example.

The training function used to update the weights and bias values is based on the scaled conjugate gradient method. The performance cross-entropy method is used for calculation, and the targets have been divided into three sets by using random indices. Initially, a survey is distributed to 20 random healthy people to collect the required data.

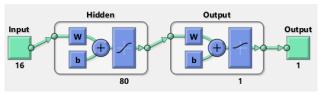


FIGURE 6. Neural Network Design.

The resultant data is used to calculate the risk using both the conventional and artificial neural network methods. The output generated is classified into five levels; very low risk, low risk, medium risk, high risk, and very high risk, which is then represented by a number, from 1 to 5. Two sets of artificial neural network methods are used in this study, based on the number of training samples.

#### III. RESULTS AND ANALYSIS

The first set of ANN method is trained with 20 samples (AI 20), and the second set is trained with 100 samples (AI 1K). This shows that the sample size in the ANN method is very important in determining the accuracy of risk percentage over the conventional method.

To test these methods, another 20 samples also have been generated and compared, based on Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical guideline heat map [8], which classify the data risk based on their GFR and ACR. The results are shown in Appendix 3 and 4.

The survey data shows that there are differences in accuracy during the classification of data using the equation and ANN. Figure 8 shows the data plotting for each method with a number of samples. The results show that there is a slight difference between the methods. The average data remains below 40% risk for healthy people. Moreover, by using the KDIGO 2012 heat map with 20 samples, the data able to mimic the results for the conventional method and ANN with a large number of training. The sensitivity and specificity of the survey data result have also been analyzed. For calculation using the equation, the sensitivity is 100%, and the specificity is 90.9%. For AI 20, the sensitivity is 88.9%, and the specificity is 63.6%. For AI 1K, the sensitivity is 66.7%, and the specificity is 90.9%.

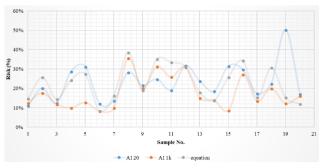


FIGURE 7. Risk Percentage and Sample Number for Survey Data.

Figure 9 shows the risk and sample for the heat map. The result shows that the accuracy of the

equation and ANN method are able to classify the risk of the samples as intended.

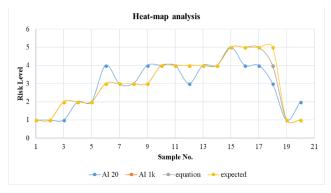


FIGURE 8. Risk Level and Sample Number for Survey Data.

Figure 10 shows the accuracy comparison between these methods. Based on the results and accuracy, it shows that the conventional method has the potential to be used as estimating only and able to estimate the risk level as intended.

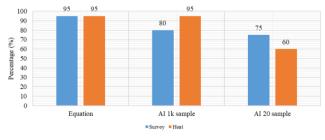


FIGURE 9. Accuracy Comparison.

The conventional method also classifies that healthy person to be in the very low-risk group while the unhealthy person to be in the very high-risk group. However, it is still not suitable for the diagnostic application.

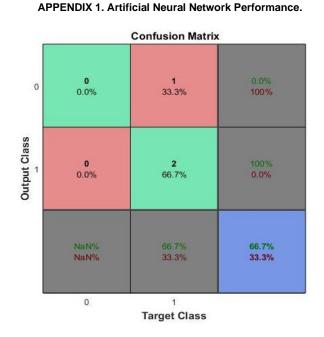
One of the methods that can be applied is the artificial neural network (ANN). The results of the artificial neural network could be improved with an increased number of samples. This shows the potential of ANN for risk estimation techniques.

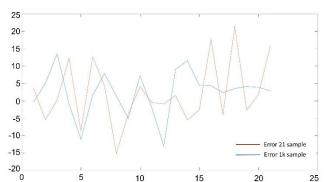
#### IV. CONCLUSION

In this study, the risk estimation of chronic kidney disease (CKD) has been generated by using retrospective data and two methods have been applied. The first method is using a conventional equation based on retrospective data and designing an equation based on the risk factors of CKD. The risk factors have been divided into three energy levels; low level, medium level, and high level, based on their effect on the nephron and cells.

The second method is to apply an artificial neural network (ANN) as one of the potential methods to improve the conventional method. The results show that the conventional method was able to generate results that are similar to the existing methods with the consideration of the other risk factors. The results also show that artificial neural network (ANN) is one of the important tools that can be utilized in order to improve the estimation accuracy. By increasing the training sample, the accuracy can be improved. This makes ANN as a potential method in risk estimation. However, more improvement is needed to be carried out to make this a practical application. One of the improvements is to train a very high large number of samples to ensure the accuracy and reliability of the network.

**APPENDIX** 





APPENDIX 2. Artificial Neural Network Comparison.

### APPENDIX 3. Survey data.

<b>F</b>										D	ata Num	ber								
Feature	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Age	23	21	22	22	53	20	26	36	75	62	53	46	63	43	36	69	26	28	36	37
Gender	Male	Fema -le	Male	Male	Male	Male	Fema -le	Male	Fema -le	Male	Male	Male	Female	Male	Male	Male	Male	Fema- le	Male	Male
Race	Cau- casi- an	Cau- casi- an	Cau- casi- an	Cau- casi- an	Cau- casi- an	African Ameri- can	Cau- casi- an	Cau- casi- an	Cau- casi- an	Cau- casi- an	Cau- casi- an	Cau- casi- an	African Ameri- can	African Ameri- can	African Ameri- can	Cau- casian	Cau- casian	Cau- casian	African Ameri- can	Cau- casian
Smoking	No	No	No	No	0	No	No	No	No	2	No	No	No	No	No	1	No	No	No	No
Water	2	3	2	3	3	2	3	2	3	2	3	3	3	2	3	2	3	3	3	3
Salt	5	6	8	7	7	4	6	4	8	6	10	12	10	8	6	10	12	10	6	10
Diabetes	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No	No
History	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Activity	Yes	No	Yes	No	No	Yes	No	No	No	No	Yes	Yes	No	Yes	No	No	Yes	No	No	Yes
Stress	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Hyperten -sion	No	No	No	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	No	No	No	No	No	Yes	No
sC	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Alb	11	5	13	15	20	12	6	28	3	17	25	21	4	10	15	18	12	20	5	4
Cr	1050	1200	1300	1000	950	1100	1800	1200	2300	900	1100	1000	1500	1150	1000	900	1200	1000	1500	1300
ACR	10	4	10	15	21	11	3	23	1	19	23	21	3	9	15	20	10	20	3	3
GFR	126	80	127	127	102	149	120	115	95	96	102	107	112	127	133	91	123	100	133	114
Equation Risk	1	2	1	2	2	1	1	2	1	2	2	2	1	1	2	2	1	2	1	1
AI 20	1	2	1	2	2	1	1	2	2	2	1	2	2	1	2	2	1	2	2	1
Al 1k	1	1	1	1	1	1	1	2	2	2	2	2	1	1	1	2	1	2	1	1
Expected	1	1	1	2	2	1	1	2	1	2	2	2	1	1	2	2	1	2	1	1

#### APPENDIX 4. Heat Map Data.

Facture-										Data I	Number									
Feature	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Age	60	21	40	35	35	75	65	79	80	76	85	68	66	72	85	75	81	92	75	42
Gender	Fema- le	Male	Fema- le	Male	Male	Male	Fema- le	Fema- le	Fema- le	Male	Male	Fema- le	Fema- le	Fema- le	Fema- le	Male	Male	Fema- le	Male	Male
Race	Cauca -sian	Cauca -sian	Afr. Ameri can	Cauca -sian	Cauca -sian	Afr. Ameri can	Afr. Ameri can	Afr. Ameri can	Afr. Ameri can	Cauca -sian	Afr. Ameri can	Cauca -sian	Afr. Ameri can	Afr. Ameri can	Afr. Ameri can	Cauca -sian	Black	Cauca -sian	Cauca -sian	Cauca- sian
Smoking	No	No	No	No	2	2	No	No	1	2	No	No	No	2	3	1	2	No	No	No
Water	4	4	4	4	2	2	2	2	2	2	2	2	3	2	1	2	1	1	4	3
Salt	3	5	3	3	5	6	3	3	5	5	5	8	10	7	10	8	12	8	3	3
Diabetes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No
History	No	No	No	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes	Yes	No	No	No	No	No
Activity	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes	Yes
Stress	No	No	No	No	No	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	No	No
Hyperten- sion	No	No	No	No	No	No	No	No	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	No	No
sC	0	1	1	1	2	1	1	1	2	1	2	1	2	3	2	5	5	6	0	1
Alb	10	5	80	240	8	180	300	250	37	230	155	300	250	40	340	285	240	30	30	5
Cr	1000	1500	800	1500	500	500	800	1000	1423	700	500	1500	1000	1600	980	750	850	1100	1600	2000
ACR	10	3	100	160	16	360	375	250	26	329	310	200	250	25	347	380	282	27	19	3
GFR	124	86	107	87	55	96	61	55	35	53	36	39	25	21	27	10	12	5	116	82
Equation Risk	1	1	2	2	2	3	3	3	3	4	4	4	4	4	5	5	5	4	1	1
AI 20	1	1	1	2	2	4	3	3	4	4	4	3	4	4	5	4	4	3	1	2
Al 1k	1	1	2	2	2	3	3	3	3	4	4	4	4	4	5	5	5	4	1	1
Expected	1	1	2	2	2	3	3	3	3	4	4	4	4	4	5	5	5	5	1	1

#### ACKNOWLEDGMENT

The authors would like to express gratitude towards University Teknologi Malaysia for providing the environment and support for the works of this study.

#### FUNDING STATEMENT

This research was not funded

#### AUTHOR CONTRIBUTIONS

Al-Amoodi Wody: Conceptualization, Data Curation, Methodology, Validation, Writing – Original Draft Preparation;

Eko Supriyanto: Project Administration, Writing – Review & Editing;

Muhammad Naqiuddin Mohd Warid: Project Administration, Supervision, Writing – Review & Editing.

#### CONFLICT OF INTERESTS

No conflict of interests was disclosed.

#### **ETHICS STATEMENTS**

Our research work follows The Committee of Publication Ethics (COPE) guideline. https://publicationethics.org.

#### REFERENCES

 US Department of Health and Human Services, Center for Disease Control and Prevention, "National Chronic Kidney Disease Fact Sheet 2017," stacks.cdc.gov. URL:

https://stacks.cdc.gov/view/cdc/46034/cdc\_46034\_DS1.pdf (Accessed 2 Sept, 2019)

- [2] N. Tangri, L. A. Stevens, J. Griffith, H. Tighiouart, O. Djurdjev, D. Naimark and A. S. Levey, "A predictive model for progression of chronic kidney disease to kidney failure," *JAMA: The Journal of the American Medical Association*, vol. 305, no. 15, pp. 1553–1559, 2011.
   DOI: https://doi.org/10.1001/jama.2011.451
- DOI: <u>https://doi.org/10.1001/jama.2011.451</u>
  [3] A. S. Levey and L. A. & Stevens, "Estimating GFR Using the CKD Epidemiology Collaboration (CKD-EPI) Creatinine Equation: More Accurate GFR Estimates, Lower CKD Prevalence Estimates, and Better Risk Predictions," *American Journal of Kidney Diseases*, vol. 55, no. 4, pp. 622–627, 2010. DOI: <u>https://doi.org/10.1053/j.ajkd.2010.02.337</u>
- [4] L. A. Inker, J. Eckfeldt, A. S. Levey, C. Leiendecker-Foster, G. Rynders, J. Manzi and J. Coresh, "Expressing the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) cystatin C equations for estimating GFR with standardized serum cystatin C Values," *American Journal of Kidney Diseases*, vol. 58, no. 4, pp. 682-684, 2011. DOI: https://doi.org/10.1053/j.ajkd.2011.05.019
- [5] L. A. Stevens, J. Manzi, A. S. Levey, J. Chen, A. E. Deysher, T. Greene, E. D. Poggio, C. H. Schmid, M. W. Steffes, Y. L. Zhang and F. Van Lente, "Impact of Creatinine Calibration on Performance of GFR Estimating Equations in a Pooled Individual Patient Database," *American Journal of Kidney Diseases*, vol. 50, no. 1, pp. 21–35, 2007. DOI: https://doi.org/10.1053/j.ajkd.2007.04.004
- [6] L. M. Pang, K. M. Tay and C. P. Lim, "Monotone fuzzy rule relabeling for the zero-order TSK fuzzy inference system", *IEEE Transactions on Fuzzy Systems*, vol. 24, no. 6, pp. 1455-1463, 2016.

DOI: https://doi.org/10.1109/TFUZZ.2016.2540059

[7] Y. W. Kerk, K. M. Tay and C. P. Lim, "An analytical interval fuzzy inference system for risk evaluation and prioritization in failure mode and effect analysis," *IEEE Systems Journal*, vol. 11, no. 3, pp. 1589-600, 2017.

- DOI: https://doi.org/10.1109/JSYST.2015.2478150
- [8] P. S. Patra, D. P. Sahu and I. Mandal, "An expert system for diagnosis of human diseases," *International Journal of Computer Applications*, vol. 1, no. 13, pp. 71-73, 2010. <u>URL:https://www.ijcaonline.org/allpdf/pxc387439.pdf</u> (Accessed: 2 Sept, 2019)
- [9] D. Pal, K. M. Mandana, S. Pal, D. Sarkar and C. Chakraborty, "Fuzzy expert system approach for coronary artery disease screening using clinical parameters," *Knowledge-Based Systems*, vol. 36, pp.162-174, 2012. DOI: https://doi.org/10.1016/j.knosys.2012.06.013
- DOI: <u>https://doi.org/10.1016/j.knosys.2012.06.013</u>
  [10] N. Allahverdi, S. Torun and I. Saritas, "Design of a fuzzy expert system for determination of coronary heart disease risk," ACM Proceedings of the 2007 International Conference on Computer Systems and Technologies, pp. 36, 2007. DOI: <u>https://doi.org/10.1145/1330598.1330638</u>
- [11] L. Á. Menéndez, F. J. de Cos Juez, F. S. Lasheras and J. Á. Riesgo, "Artificial neural networks applied to cancer detection in a breast screening programme," *Mathematical and Computer Modelling*, vol. 52, no. 7-8, pp. 983-991, 2010. DOI: https://doi.org/10.1016/j.mcm.2010.03.019
- [12] M. R. Pooja and M. P. Pushpalatha, "A Neural Network Approach for Risk Assessment of Asthma Disease," *Journal* of *Health Informatics & Management*, vol. 2, no. 1, 2018. URL: <u>https://www.scitechnol.com/abstract/a-neural-networkapproach-for-risk-assessment-of-asthma-disease-7819.html</u> (Accessed: 2 Sept, 2019)
- [13] S. Agrawal and J. Agrawal, "Neural network techniques for cancer prediction: A survey," *Procedia Computer Science*, vol. 60, pp. 769-774, 2015.

DOI: https://doi.org/10.1016/j.procs.2015.08.234

[14] M. Catalogna, E. Cohen, S. Fishman, Z. Halpern, U. Nevo and E. Ben-Jacob, "Artificial neural networks based controller for glucose monitoring during clamp test," *PLoS ONE*, vol. 7, no. 8, pp. e44587, 2012.

DOI: https://doi.org/10.1371/journal.pone.0044587

- [15] E. Elveren and N. Yumuşak, "Tuberculosis disease diagnosis using artificial neural network trained with genetic algorithm," *Journal of Medical Systems*, vol. 35, no. 3, pp. 329-332, 2011. DOI: <u>https://doi.org/10.1007/s10916-009-9369-3</u>
- [16] D. C. Barbosa, D. B. Roupar, J. C. Ramos, A. C. Tavares and C. S. Lima, "Automatic small bowel tumor diagnosis by using multi-scale wavelet-based analysis in wireless capsule endoscopy images," *Biomedical Engineering Online*, vol. 11, no. 1, pp. 3, 2012. DOI: https://doi.org/10.1186/1475-925X-11-3
- [17] Y. Li, A. M. Rauth and X. Y. Wu, "Prediction of kinetics of doxorubicin release from sulfopropyl dextran ion-exchange microspheres using artificial neural networks," *European Journal of Pharmaceutical Sciences*, vol. 24, no. 5, pp. 401-410, 2005.

DOI: <u>https://doi.org/10.1016/j.ejps.2004.12.005</u>

[18] J. Coresh, E. Selvin, L. A. Stevens, J. Manzi, J. W. Kusek, P. Eggers, F. Van Lente and A. S. Levey, "Prevalence of chronic kidney disease in the United States," *JAMA*, vol. 298, no. 17, pp. 2038–2047, 2007.

DOI: https://doi.org/10.1001/jama.298.17.2038

[19] R. D. Lindeman, J. Tobin and N. W. Shock, "Longitudinal studies on the rate of decline in renal function with age," *Journal of the American Geriatrics Society*, vol. 33, no. 4, pp. 278-285, 1985.

DOI: https://doi.org/10.1111/j.1532-5415.1985.tb07117.x

- [20] G. Süleymanlar, C. Utaş, T. Arinsoy, K. Ateş, B. Altun, M. R. Altiparmak, T. Ecder, M. E. Yilmaz, T. Çamsari, A. Başçi and K. Serdengeçti, "A population-based survey of Chronic Renal Disease In Turkey—the CREDIT study," *Nephrology Dialysis Transplantation*, vol. 26, no. 6, pp. 1862-1871, 2010. DOI: <u>https://doi.org/10.1093/ndt/gfq656</u>
- [21] I. Goldberg and I. Krause, "The role of gender in chronic kidney disease," *European Medical Journal*, vol. 1, no. 2, pp. 58-64, 2016.
   DOI: https://doi.org/10.33590/emj/10312319
- [22] A. S. Levey, L. A. Stevens, C. H. Schmid, Y. L. Zhang, A. F. Castro, H. I. Feldman, J. W. Kusek, P. Eggers, F. Van Lente, T. Greene and J. Coresh, "A new equation to estimate glomerular filtration rate," *Annals of Internal Medicine*, vol. 150, no. 9, pp. 604-612, 2009.

DOI: <u>https://doi.org/10.7326/0003-4819-150-9-200905050-</u>00006

[23] United States Renal Data System, "2015 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States," usrds.org.

URL: <u>http://www.usrds.org/adr.aspx</u> (accessed 20 Dec, 2018).

[24] K. B. Werner, S. Elmståhl, A. Christensson and M. Pihlsgård, "Male sex and vascular risk factors affect cystatin C-derived renal function in older people without diabetes or overt vascular disease," *Age and Ageing*, vol. 43, no. 3, pp. 411-417, 2013.

DOI: https://doi.org/10.1093/ageing/aft191

- [25] D. Nitsch, D. F. Dietrich, A. von Eckardstein, J. M. Gaspoz, S. H. Downs, P. Leuenberger, J. M. Tschopp, O. Brändli, R. Keller, M. W. Gerbase and N. M. Probst-Hensch, "Prevalence of renal impairment and its association with cardiovascular risk factors in a general population: results of the Swiss SAPALDIA study," *Nephrology Dialysis Transplantation*, vol. 21, no. 4, pp. 935-944, 2006. DOI: <u>https://doi.org/10.1093/ndt/gfk021</u>
- [26] W. W. Brown, R. M. Peters, S. E. Ohmit, W. F. Keane, A. Collins, S. C. Chen, K. King, M. J. Klag, D. A. Molony and J. M. Flack, "Early detection of kidney disease in community settings: the Kidney Early Evaluation Program (KEEP)," *American Journal of Kidney Diseases*, vol. 42, no. 1, pp. 22-35, 2003.

DOI: https://doi.org/10.1016/S0272-6386(03)00405-0

- [27] S. J. Chadban, E. M. Briganti, P. G. Kerr, D. W. Dunstan, T. A. Welborn, P. Z. Zimmet and R. C. Atkins, "Prevalence of kidney damage in Australian adults: The AusDiab kidney study," *Journal of the American Society of Nephrology*, vol. 14, no. suppl 2, pp. S131-S138, 2003. DOI: https://doi.org/10.1097/01.ASN.0000070152.11927.4A
- [28] M. E. Tarver-Carr, N. R. Powe, M. S. Eberhardt, T. A. LaVeist, R. S. Kington, J. Coresh and F. L. Brancati, "Excess risk of chronic kidney disease among African-American versus white subjects in the United States: a population-based study of potential explanatory factors," *Journal of the American Society* of Nephrology, vol. 13, no. 9, pp. 2363-2370, 2002. DOI: https://doi.org/10.1097/01.ASN.0000026493.18542.6A
- [29] P. Muntner, B. Newsome, H. Kramer, C. A. Peralta, Y. Kim, D. R. Jacobs, C. I Kiefe and C. E. Lewis, "Racial differences in the incidence of chronic kidney disease," *Clinical Journal of the American Society of Nephrology*, vol. 7, no. 1, pp. 101-107, 2012.

DOI: https://doi.org/10.2215/CJN.06450611

- [30] E. Y. Song, W. M. McClellan, A. McClellan, R. Gadi, A. C. Hadley, J. Krisher, M. Clay and B. I. Freedman, "Effect of community characteristics on familial clustering of end-stage renal disease," *American Journal of Nephrology*, vol. 30, no. 6, pp. 499-504, 2009. DOI: <u>https://doi.org/10.1159/000243716</u>
- [31] W. M. McClellan, D. G. Warnock, S. Judd, P. Muntner, R. E. Patzer, B. D. Bradbury, L. A. McClure, B. B. Newsome and G. Howard, "Association of family history of ESRD, prevalent albuminuria, and reduced GFR with incident ESRD," *American Journal of Kidney Diseases*, vol. 59, no. 1, pp. 25-31, 2012.

DOI: https://doi.org/10.1053/j.ajkd.2011.09.018

- [32] K. Matsushita, B. K. Mahmoodi, M. Woodward, J. R. Emberson, T. H. Jafar, S. H. Jee, K. R. Polkinghorne, A. Shankar, D. H. Smith, M. Tonelli and D. G. Warnock DG, "Comparison of risk prediction using the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate," *JAMA*, vol. 307, no. 18, pp. 1941-1951, 2012. DOI: <u>https://doi.org/10.1001/jama.2012.3954</u>
- [33] L. A. Inker, B. C. Astor, C. H. Fox, et al., "KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD," *American journal of kidney diseases: the official journal of the National Kidney Foundation*, vol. 63, no. 5, pp. 713-755, 2014. DOI: <u>https://doi.org/10.1053/j.ajkd.2014.01.416</u>
- [34] A. Chang and H. Kramer, "Should eGFR and Albuminuria Be Added to the Framingham Risk Score Chronic Kidney Disease and Cardiovascular Disease Risk Prediction," *Nephron Clinical Practice*, vol. 119, no. 2, pp. c171-c178, 2011.

DOI: https://doi.org/10.1159/000325669

- F. W. Spierto, W. H. Hannon, E. W. Gunter and S. J. Smith, "Stability of urine creatinine," *Clinica Chimica Acta*, vol. 264, no. 2, pp. 227-232, 1997. DOI: <u>https://doi.org/10.1016/S0009-8981(97)00080-6</u>
- [36] R. G. Nelson and K. R. Tuttle, "The new KDOQITM clinical practice guidelines and clinical practice recommendations for diabetes and CKD," *Blood Purification*, vol. 25, no. 1, pp. 112-114, 2007.

DOI: https://doi.org/10.1159/000096407

- [37] A. Chockalingam, N. R. Campbell and J. G. Fodor, "Worldwide epidemic of hypertension," *Canadian Journal of Cardiology*, vol. 22, no. 7, pp. 553-555, 2006. DOI: https://doi.org/10.1016/s0828-282x(06)70275-6
- DOI: <u>https://doi.org/10.1016/s0828-282x(06)70275-6</u>
  [38] M. V. Rao, Y. Qiu, C. Wang and G. Bakris, "Hypertension and CKD: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES), 1999-2004," *American Journal of Kidney Diseases*, vol. 51, no. 4, pp. S30-S37, 2008.

DOI: https://doi.org/10.1053/j.ajkd.2007.12.012

[39] J. M. Sontrop, S. N. Dixon, A. X. Garg, I. Buendia-Jimenez, O. Dohein, S. H. Huang and W. F. Clark, "Association between water intake, chronic kidney disease, and cardiovascular disease: a cross-sectional analysis of NHANES data," *American Journal of Nephrology*, vol. 37, no. 5, pp. 434-442, 2013.

DOI: https://doi.org/10.1159/000350377

[40] R. Yacoub, H. Habib, A. Lahdo, R. Al Ali, L. Varjabedian, G. Atalla, N. K. Akl, S. Aldakheel, S. Alahdab and S. Albitar, "Association between smoking and chronic kidney disease: a case control study," *BMC Public Health*, vol. 10, no. 1, pp. 731, 2010.

DOI: https://doi.org/10.1186/1471-2458-10-731

- [41] S. L. Rodrigues, P. R. Souza Júnior, E. B. Pimentel, M. P. Baldo, D. C. Malta, J. G. Mill and C. L. Szwarcwald, "Relationship between salt consumption measured by 24-h urine collection and blood pressure in the adult population of Vitória (Brazil)," *Brazilian Journal of Medical and Biological Research*, vol. 48, no. 8, pp. 728-735, 2015. DOI: <u>https://doi.org/10.1590/1414-431x20154455</u>
- [42] C. Crump, J. Sundquist, M. A. Winkleby and K. Sundquist, "Low stress resilience in late adolescence and risk of hypertension in adulthood," *Heart*, vol. 102, no. 7, pp. 541-547, 2016.
   DOI: https://doi.org/10.1136/heartinl-2015-308597
- K. M. Diaz and D. Shimbo, "Physical activity and the prevention of hypertension," *Current Hypertension Reports*, vol. 15, no. 6, pp. 659-668, 2013.
   DOI: https://doi.org/10.1007/s11906-013-0386-8