hasil cek_endang darmawan

by Endang Darmawan

Submission date: 16-Jun-2021 04:06PM (UTC+0700)
Submission ID: 1607399421
File name: ression_Interaction_Model_Simeftiany_Indrilemta_Lomo_1_1_1.docx (192.88K)
Word count: 4587
Character count: 25019

A Survival Analysis with Cox Regression Interaction Model of Type II Diabetes Mellitus in Indonesian

[a]Simeftiany Indrilemta Lomo,Sugiyarto* [b],Endang Darmawan [c]

[a,c]Faculty of Pharmacy, Ahmad Dahlan University, 55164, Yogyakarta, Indonesia
[b]Faculty of Applied Science and Technology, Ahmad Dahlan University, 55191, Bantul, Indonesia
*E-mail: sugiyarto@math.uad.ac.id

Abstract

Background: Type II diabetes mellitus is a metabolic syndrome characterized by hyperglycemia. Diabetes is still one of the world's health threats where the number of people with disabilities and mortality rates continue to increase over time. This study aims to analyze the survival of patients with type II diabetes mellitus as well as factors that affect it using survival analysis.

Methods: This study used medical record data of type II diabetes mellitus patients undergoing treatment for the period 2015-2019 at PKU Muhammadiyah Gamping Hospital and PKU Muhammadiyah Hospital Yogyakarta. The survival analysis was conducted by Kaplan Meier curves and cox regression equations of interaction models.

Results: In this study, there were 1293 patients with type II diabetes mellitus, with 10.36% (*n* = 134 patients) death. Patients aged ≥45 years 88.86% (*n* = 1149), 53.29% women (*n* = 689), 71.15% (*n* = 920) with comorbidities, 56.84% (*n* = 735) high blood glucose levels, and 49.03% (*n* = 634) received a combination of insulin-oral antidiabetic therapy. Factors related to the patient's survival are the interaction of gender variables with age variables (p <0.05; HR = 0.841; CI 95% 0.711-0.993), variable interaction of blood glucose levels while with variable age (p <0,05; HR = 1,061; CI 95% 1,028-1,096), variable interaction of blood glucose levels with comorbidity variables (p <0,05; HR 1,221; CI 95% 1,036-1,438), and variable interaction of blood glucose levels with variable treatment profiles (p <0,05; HR = 0.824; CI 95% 0.747-0.909).

Conclusions: Factors that affect the survival of patients with type II diabetes mellitus are age, gender, diagnose complications, comorbidity, intermittent blood glucose levels, and treatment profiles.

Keywords: Mortality, Risk factors, Survival analysis, Type II diabetes mellitus

Background

Type II diabetes mellitus is a group of metabolic diseases with characteristic hyperglycemia[1] that occur due to abnormalities of insulin secretion, insulin work or both[2]. This disease is one of the world's health threats, including Indonesia. Based on basic health research data in 2018, the prevalence of diabetes mellitus in the ≥15-year-old population in Indonesia increased from 1.5% in 2013 to 2.0% in 2018 [3]. WHO estimates that people with diabetes mellitus will continue to increase up to 2-3 times by 2035 [4]. Patients aged 20-79 are expected to increase to 642 million with most being in low- and middle-income countries [5].

The mortality rate due to diabetes mellitus ranges from 0.28-8.24 per 100 patients-years with the highest mortality in older patients and longer [6]. The IDF said 5.0 million deaths occurred in 2015 with 415 million [5]. Diabetic mellitus patients who have complications with hypertension and poor blood glucose control have a higher risk of failure [7]. Not only that, renal complications [7]–[10], cardiovascular[7], [11]–[13], and peripheral circulation [14], [15] also increase the risk of mortality of type II diabetes mellitus patients.

Survival analysis is a statistical technique that has been widely used in health sciences [16]–[18] to analyze the chances of death, recurrence, survival and other events at any given time [19]. Accurate predictions regarding the externality or survival rate of diabetic patients can be key to stratification of prognosis and therapy. This study was conducted to assess the length of life, therapy and factors that affect survival so that it is expected to have a linear impact with the length of life of diabetes mellitus patients.

Methods

Design and settings

This research is a descriptive research, where the data used is the medical record data of patients with type II diabetes mellitus who undergo hospitalization and outpatient at two hospitals namely PKU Muhammadiyah Gamping Hospital and PKU Muhammadiyah Hospital Yogyakarta, Indonesia. Inclusion criteria: Patients diagnosed with Type II Diabetes Mellitus who are ≥18 years old and undergo treatment during the period 2015 to 2019. Patients diagnosed with Type I diabetes mellitus and gestational diabetes as well as illegible medical records and incomplete data will be excluded.

Data retrieval was conducted retrospectively, by collecting all data related to this study, from the initial events of patients diagnosed with type II diabetes mellitus to the observation period. It aims to determine the survival of patients with type II diabetes mellitus and the factors that affect it. The patient's survival is known based on the patient's survival status (life/death) and survival time measured from the time the patient was diagnosed with type II diabetes mellitus until the time the data was taken. The required data are patient name, gender, age, history of disease, complications, when first diagnosed with Diabetes Mellitus type II, therapy regimen used and laboratory results in the form of blood glucose levels during. This research has obtained ethical clearance from the Research Ethics Commission of PKU Muhammadiyah Hospital Yogyakarta No. 0011/KT.7.4/VIII/2020.

Variable

In this study there are several research variables, namely patient survival status, survival time, gender (X1), age (X2), concomitant disease (X3), complications (X4), treatment profile (X5), and current blood glucose levels (X6). The data that has been obtained is classified and coded according to existing variables. Variables of patient survival status, gender, and accompanying disease are grouped into dichotomical data. Survival time is expressed in units of years. In the age variable is grouped into 2 levels namely <45 years and ≥45 years. Variable complications are divided into: without complications, renal complications, peripheral circulation complications, multicomplication, coma, cardiovascular complications, and other complications. The variable profile of treatment is divided into insulin, oral antidiabetics, and a combination of oral insulin-antidiabetics. Variable blood glucose levels when divided into: Normal (<140 mg/dL), Moderate (140-199 mg/dL), and High (≥ 200 mg/dL).

Statistical analysis

In this journal, Kaplan Meier method is used to know the characteristics of survival time. In addition, the Log Rank test was used to determine the difference in survival curve between groups of factors that affect the survival of patients with type II diabetes mellitus with $p < 0.05$. Proportional hazard assumption testing is conducted with two tests, namely visual test using Kaplan Meier method and formal test using Goodness of fit test. The entire covariate result of cox regression p<0.05 is included in the equation model. The data was analyzed using SPSS 25 software.

Results

In this study there were 1293 data of type II diabetes mellitus patients 10.36% (n = 134) were non-survivor patients or died and 89.64% (n = 1159) were survivor patients or still surviving during the period 2015-2019. In non-survivor patients there were 70 male patients while 64 patients were female, 126 patients were ≥45 years old, 76 patients were diagnosed with complications, 109 patients were recorded with comorbidity, with moderately high blood glucose levels.

Based on research that has been done obtained data on the overall number of patients with type II diabetes mellitus aged ≥45 years more (88.86%) than patients who are <45 years old. In the sex variables obtained 53.29% of type II diabetes mellitus patients were female while 46.71% were male. The most common complications are peripheral circulation complications. The majority of patients had comorbidity (71.15%) and 56.84% of type II diabetes mellitus patients had high blood glucose levels. 49.03% of patients received insulin-oral antidiabetic combination therapy, 44.01% received oral antidiabetic therapy, and 6.96% received insulin therapy.

Hazard proportional assumption testing is conducted with 2 tests, namely visual test and formal test. The visual test was conducted using Kaplan Meier's curve approach. A feature of a survival curve that meets the PH assumption is that the survival line on the Kaplan Meier curve between groups does not intersect. Based on the results of survival analysis with using kaplan meier curve obtained lines that intersect between groups / categories on all variables (Figure 1a, Figure 1b, Figure 1c, Figure 1d, Figure 1e, Figure 1f), so it does not meet the assumption of PH.

Table I. Frequency Distribution of Characteristics of Type II Diabetes Mellitus Patients at PKU Muhammadiyah Gamping Hospital and Yogyakarta City

Variable	*n*	(%)
Survival Status		
• Life	1159	89,64
• Died	134	10,36
Gender		
• Male	604	46,71
• Women	689	53,29
Age		
• <45 years old	144	11,14
• ≥45 years old	1149	88,86
Diagnosis of Complications		
• Without Complications	719	55,61
• Renal Complications	56	4,33
• Neurology Complications	171	13,23
• Peripheral Circulation Complications	199	15,39
• Multikomplikasi	37	15,39
• Coma	34	2,63
• Cardiovascular Complications	76	5,33
• Other Complications	1	0,08
Comorbidity		
• Without Comorbidity	373	28,85
• With Comorbidity	920	71,15
Treatment Profile		
• Insulin	90	6,96
• Oral antidiabetics	569	44,01
• Combination	634	49,03
Blood Glucose Levels		
• Normal	102	7,89
• Moderate	456	35,27
• High	735	56,84

Table II. *Goodness of Fit* Test Results of Type II Diabetes Mellitus Patients at PKU Muhammadiyah Gamping Hospital and Yogyakarta City

	Therapy	**Gender**	**Age**	**Diagnosis of Complications**	**Comorbidity**	**Blood glucose** levels **(mg/dL)**
Chi-Square	409,592	5,588	781,148	2402,227	231,407	467,012
Df	2	1	1	7	1	2
Asymp. Sig	0,000	0,018	0,000	0,000	0,000	0,000

Keterangan: df = *degree of freedom*

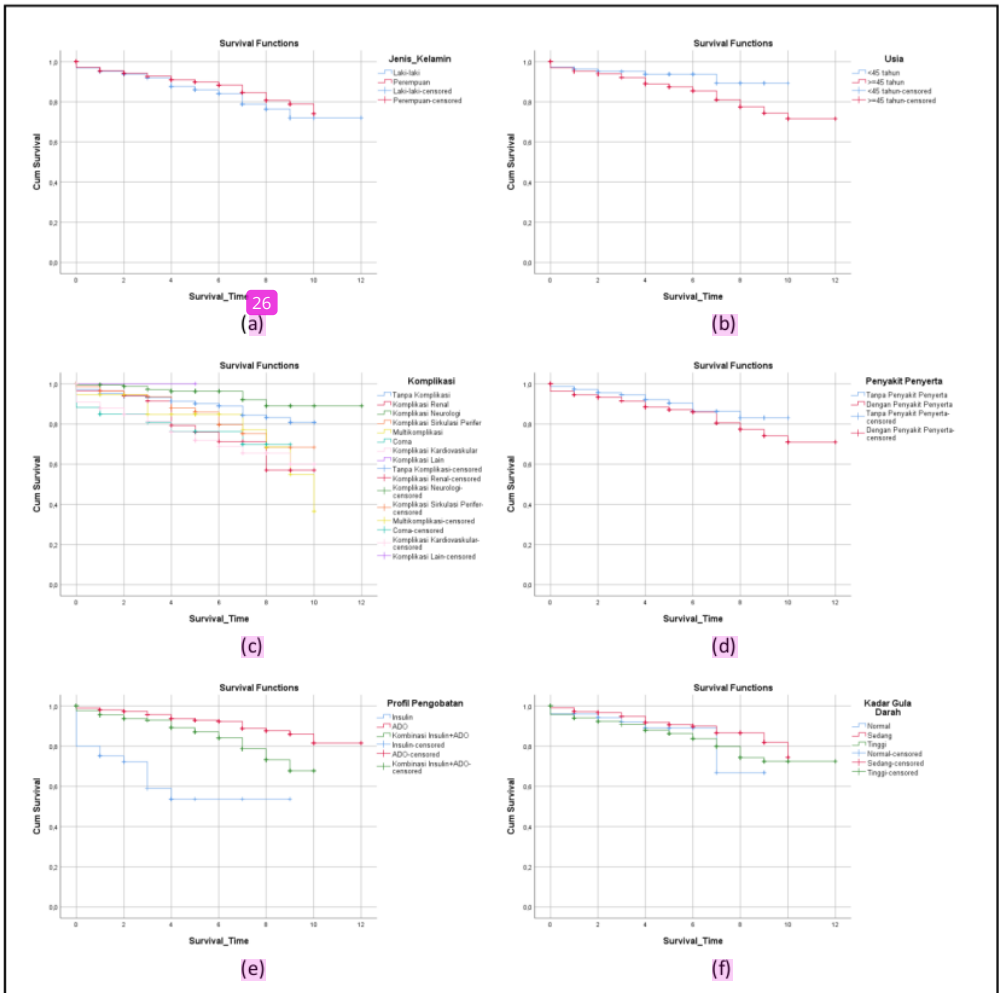

Figure 1. Kaplan Meier curves each factor. (a) Gender; (b) Age; (c) Complications; (d) Comorbidity; (e) Treatment Profile; (f) Blood Glucose Levels.

Table III. Cox Regression Results of Type II Diabetes Mellitus Patient Interaction Model at PKU Muhammadiyah Gamping Hospital and Yogyakarta City

	B	SE	df	Sig.	Exp(B)	95,0% CI for Exp(B)	
						Lower	Upper
Sex*Age	-0,174	0,085	1	0,041	0,841	0,711	0,993
Blood Glucose Levels *Age	0,337	0,092	1	0,000	1,401	1,169	1,678
Complications*Treatment Profile	0,059	0,016	1	0,000	1,061	1,028	1,096
Blood Glucose Levels *Comorbidity	0,199	0,083	1	0,017	1,221	1,036	1,438
Blood Glucose Levels *Treatment Profile	-0,193	0,050	1	0,000	0,824	0,747	0,909

Description: B = Slope Value or Beta Coefficient of Constants; SE = *Standard Error*; df = degree *of freedom*; Sig. = Significance or *p*-value Wald test; Exp(B) = Exponential Beta Coefficient

Hazard proportional assumption testing is also conducted with the Goodness of Fit test approach. This test is conducted to obtain more objective decisions. In this test, H_0 means factors that are suspected to affect the survival of patients with diabetes mellitus type II meet the assumption of proportional hazard, while H_1 means that factors that are suspected to affect the survival of patients with type II diabetes mellitus do not meet the assumption of proportional hazard. Reject decision H0 if p-value < α = 5%. Here are the results of hazard proportional assumption test using Goodness of Fit test. Based on table II it can be concluded that all variables do not meet hazard proportional assumptions, because the significance value of all variables is less than the α value of 0.05.

Based on the analysis, the variables related to the survival of Type II Diabetes Mellitus patients are the interaction of gender variables with age variables (p<0.05; HR = 0.841; CI 95% 0.711-0.993), variable interaction of blood glucose levels during with variable age (p <0.05; HR = 1,061; CI 95% 1,028-1,096), variable interaction of blood glucose levels when with concomitant disease variables (p <0.05; HR 1,221; CI 95% 1,036-1,438), and variable interaction of blood glucose levels with variable treatment profiles (p <0.05; HR = 0.824; CI 95% 0.747-0.909).

Discussion

The analysis using the Kaplan-Meier survival curve aims to find out an overview of the characteristics of survival time. In addition, the Kaplan Meier curve is also used to assess proportional hazard assumptions. To see the difference in survival curve can be done statistically testing by using Log Rank test. Log-Rank test is intended to determine the difference in survival curve between groups of factors that affect the survival of patients with type II diabetes mellitus. In addition to using the Kaplan Meier curve, to see the difference in survival curve can be done statistically testing by using *Log Rank* test. Test value of 2.010 with a degree of freedom of 1 and *p*-value of Log *Rank* test result of 0.156. The results of this test will be compared to the α value of 5%. The *p*-value value is greater than the α hence the decision to accept H_0 which means there is no difference in *the survival* curve based on gender.

Based on Figure 1a shows the curve position of type II diabetes mellitus patients who are female and male close to each other in the 0th to 3rd year. In year 4, the curve position of the patient with the male gender is below the curve of the female patient. This states that in the 0th to 3rd year, both women and men have a relatively similar level of survival probability, while in the 4th year the probability of survival of male patients is lower than that of female patients, so descriptively there is a difference in the survival curve of type II diabetes mellitus patients based on the gender suffered

Kaplan Meier's curve in Figure 1 shows the curve position of patients diagnosed with type II diabetes mellitus at the age of ≥45 years is below the curve of patients who are recorded as diagnosed with type II diabetes mellitus aged <45 years. The <45 years old patient curve also showed a fairly slow decline and until the 10th year was still above 0.8. These results state that the probability of survival of patients diagnosed at the age of <45 years is higher than patients diagnosed with type II diabetes mellitus at the age of ≥45 years.

In the analysis using Log Rank test, obtained a result of 2,899 with a degree of freedom of 1 and p-value of 0.089. This result is then compared to α by 5%, then obtained a p-value greater than α, so the decision to accept H0, which means there is no difference in the survival curve of type II diabetes mellitus patients based on the initial age of diagnosis.

Based on Figure 1c, the curve of a multi-diagnosed patient is at the very bottom when compared to the curve of the patient diagnosed with other complications. This indicates that patients with multicomplication have a lower probability of survival than other complications. Statistically, *the Log Rank* test obtained 36,627 with a degree of freedom of 7 and *p*-value of 0.000. This value is compared to the α value of 5%. The results showed that the value of *p*-value is smaller than α, hence the decision to reject H_0 which means there is a difference in the *survival* curve of type II diabetes mellitus patients based on complications suffered.

Figure 1d shows the curve position of type II diabetes mellitus patients who have comorbidity below the curve of type II diabetes mellitus patients without comorbidity. It appears that the survival curve of patients without comorbidity is above 0.8 while the survival curve of patients who have comorbidity continues to decrease below the line of 0.8, so descriptively, the probability of survival of type II diabetes mellitus patients without comorbidity is better compared to patients with type II diabetes mellitus with comorbidity. However, based on statistics, *the Log Rank* test with a result of 3,444, a degree of freedom of 1, and a value of *p*-value of 0.064, where the value of *p*-value is greater than the value of α 5%, states that there is no difference in the curve of type II diabetes mellitus patients based on comorbidity.

Based on Figure 1e, the curve position of type II diabetes mellitus patients receiving insulin therapy is well below the curve of type II diabetes mellitus patients who receive oral antidiabetics as well as type II diabetes mellitus patients who receive insulin-oral antidiabetic combination therapy. This indicates that the survival of patients receiving insulin therapy is lower compared to patients receiving oral antidiabetics or a combination of insulin-oral antidiabetics. The curve of patients receiving oral antidiabetic therapy dropped quite slowly until the 10th year was still above the 0.8 line. This means the probability of survival of type II diabetes mellitus patients receiving oral antidiabetic therapy is high. Statistical analysis using *Log Rank* shows a test result of 117.655 with a degree of freedom of 2 and a value *of p*-value of 0.001. This value is then compared to the α value of 0.05%. The results showed a value of *p*-value less than the value of α so the decision to reject H_0 which means there is a difference in *the survival* curve of type II diabetes mellitus patients based on the profile of treatment.

In Figure 1f, the curve position of type II diabetes mellitus patients who have normal blood glucose levels is below the curve of type II diabetes mellitus patients who have moderate and high blood glucose levels. These results show the survival of type II diabetes mellitus patients who have normal blood glucose tend to be low. In statistical analysis, *log* rank test results were obtained 7,793 with a degree of freedom of 2 and a *p*-value value of 0.020. This value is then compared with a α value of 5%, where the *p-value* is less than α, so the decision to reject H_0 which means there

is a difference in the *survival* curve of type II diabetes mellitus patients based on current blood glucose levels.

The table shows that every one year of age increase in type II diabetes mellitus patients both male and female, the probability of death increases by 0.841 times. Meanwhile, every one year of diabetes mellitus type II patients followed by consistently high blood glucose levels, the probability of death increased by 1,401 times. Sanusi *et al.* in his research stated that the younger the patient's age, the longer his lifesurance time will be. Patients under the age of 45 had a 0.015 times lower risk of failure than patients over the age of 45 [20]. Shaik *et al.* states if the age of diabetic patients increases then the risk of death also increases simultaneously [21]. Based on blood glucose levels, patients with high blood glucose levels had a 1,128 times greater risk of failure than patients with low/normal blood glucose levels. Dewi *et al.* also stated that patients with type II diabetes mellitus who have high and low blood glucose levels have a 1,587 times faster risk than patients with normal/stable blood glucose levels. In addition, female type II diabetes mellitus patients had a 1,557-fold risk of failure compared to male type II diabetes mellitus patients [22]. The amount of comparison between the composition of estradiol will make the estrogen receptor gene (ER) and estradiol receptor in women will be activated, it causes the metabolic process will work and both genes will coordinate in insulin sensitivity and increased glucose uptake in the blood. In line with the increasing age of humans, the hormone estrogen will decrease causing insulin sensitivity and blood glucose uptake will drop [23].

Patients with complications and received a treatment profile of insulin combination therapy + oral antidiabetics, the probability of experiencing the event of death 1,061 times. The hazard ratio for interaction of blood glucose levels during and treatment profile was 0.824, which means patients with current blood glucose levels and receiving insulin-oral antidiabetic combination therapy have a 0.824 chance of dying compared to patients with normal/moderate blood glucose levels and receiving oral/insulin antidiabetic therapy. In addition, the probability of death of patients with high blood glucose levels and comorbidity increased by 1,221 times compared to patients who had normal blood glucose levels and without comorbidity. Research Dewi *et al.* stated that patients with type II diabetes mellitus without concomitant disease had a 0.640 times slower risk of failure than type II diabetes mellitus patients with concomitant disease [22]. Another study conducted by Putri stated the chances of diabetes mellitus patients who did not have another diagnosis 3.60 times compared to diabetes mellitus patients who had a diagnosis of lain [24].

Research shows that 84.1% of type II diabetes mellitus patients with complications have a poor quality of life and, the longer the patient has diabetes, the higher the risk of [25] On the other hand, Derebew stated that patients who received only oral antidiabetic therapy and patients who received oral antidiabetic therapy combined with insulin had a longer recovery time than patients who received only insulin therapy [26]. Combination therapy with multitarget more provides the benefits of treatment achieved aggressively. According to the Directorate General of Pharmaceutical and Medical

Devices, the combination of insulin-oral antidiabetic and the combination between oral antidiabetic is used to obtain controlled blood glucose effects at all times and minimize side effects as well as reduce the risk of acute complications and inhibit the progression of microangiopathy and macroangiopathy [27].

Table IV. Survival Table *of* Type II Diabetes Mellitus Patients at PKU Muhammadiyah Gamping Hospital and Yogyakarta City

Time (year)	H(*t*)	S(*t*)
0	0,017	0,973
1	0,027	0,959
2	0,035	0,947
3	0,045	0,933
4	0,063	0,908
5	0,071	0,896
6	0,082	0,880
7	0,109	0,844
8	0,130	0,817
9	0,148	0,795
10	0,165	0,775

Description: H(*t*) = *hazard* function; S(*t*) = *survival* function

Based on table IV, hazard H(t) function shows that patients with type II diabetes mellitus in the 0th to 10th year have increased meaning that the risk of patients to experience failure (death) is higher. In survival function S(t) from year 0 to year 10 decreased means the probability of survival of the patient is lower. This is not in accordance with the research conducted by Putri which states that the longer the patient suffers from diabetes mellitus, the higher the patient's survival ability to diabetes mellitus [24]. The greater the t value, the smaller the S(t) value, while the cumulative hazard indicates that the greater the t time, the greater the H(t) value will tend to be the greater. This means that the probability of the patient surviving until t time will be smaller (close to zero) and the risk of dying will be greater [28].

The models or formulas for predicting hazard functions and survival functions are as follows.

a. Hazard Function

$$H(t) = H0(t)\, e^{Y} \quad (1)$$

$$H(t) = H0(t)\, e^{0.337\,(X6-X2)\,-0.199\,(X6-X3)-0.059\,(X4-X6)-0,174\,(X1-X2)-0.193\,(X6-X5)}$$

b. Survival Function

$$S(t) = S0(t)^{(e^{\wedge}y)} \quad (2)$$

$$S(t) = S0(t)^{e^{\wedge}0,337(X6*X2)+0,199(X6*X3)+0,059(X4*X6)-0,174(X1*X2)-0,193(X6*X5)}$$

Conclusions

Factors that affect the survival of patients with type II diabetes mellitus are gender, age, diagnosis of complications, comorbidity, intermittent blood glucose levels, and treatment profile.

References

[1] Y. Z. Guangcui Xu, "Type 2 Diabetes Mellitus- Disease, Diagnosis and Treatment," *J. Diabetes Metab.*, vol. 06, no. 05, 2015, doi: 10.4172/2155-6156.1000533.

[2] J. S. Skyler *et al.*, "Differentiation of diabetes by pathophysiology, natural history, and prognosis," *Diabetes*, vol. 66, no. 2, pp. 241–255, 2017, doi: 10.2337/db16-0806.

[3] Kemenkes RI, "Laporan Hasil Riset Kesehatan Dasar (Riskesdas) Indonesia tahun 2018," *Riset Kesehatan Dasar 2018*. pp. 182–183, 2018.

[4] World Health Organization, "Global Report on Diabetes," *World Heal. Organ.*, vol. 978, pp. 6–86, 2016, [Online]. Available: http://www.who.int/about/licensing/copyright_form/index.html%0Ahttp://www.who.int/about/licensing/copyright_form/index.html%0Ahttps://apps.who.int/iris/handle/10665/204871%0Ahttp://www.who.int/about/licensing/.

[5] K. Ogurtsova *et al.*, "IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040," *Diabetes Res. Clin. Pract.*, vol. 128, no. July 2018, pp. 40–50, 2017, doi: 10.1016/j.diabres.2017.03.024.

[6] E. Barkoudah, H. Skali, H. Uno, S. D. Solomon, and M. A. Pfeffer, "Mortality Rates in Trials of Subjects With Type 2 Diabetes," *J. Am. Heart Assoc.*, vol. 1, no. 1, pp. 1–8, 2012, doi: 10.1161/jaha.111.000059.

[7] A. S. Pambudi and S. Pramana, "Survival Analysis of Patient Diabetes Mellitus Type II with Complication (Study Case of Medical Record from 2012 to 2015 in General Hospital of Dr. Moewardi Surakarta)," *Adv. Sci. Lett.*, vol. 24, no. 9, pp. 6882–6885, 2018, doi: 10.1166/asl.2018.12872.

[8] P. Bramlage *et al.*, "Patient and disease characteristics of type-2 diabetes patients with or without chronic kidney disease: An analysis of the German DPV and DIVE databases," *Cardiovasc. Diabetol.*, vol. 18, no. 1, pp. 1–12, 2019, doi: 10.1186/s12933-019-0837-x.

[9] J. A. Gimeno-Orna, Y. Blasco-Lamarca, B. Campos-Gutierrez, E. Molinero-Herguedas, L. M. Lou-Arnal, and B. García-García, "Risk of mortality associated to chronic kidney disease in patients with type 2 diabetes mellitus: A 13-year follow-up," *Nefrologia*, vol. 35, no. 5, pp. 487–492, 2015, doi: 10.1016/j.nefroe.2015.09.012.

[10] S. De Cosmo *et al.*, "Predictors of chronic kidney disease in type 2 diabetes," *Medicine (Baltimore).*, vol. 95, no. 27, p. e4007, 2016, doi: 10.1097/md.0000000000004007.

[11] A. M. Schmidt, "Diabetes Mellitus and Cardiovascular Disease," *Arterioscler. Thromb. Vasc. Biol.*, vol. 39, no. 4, pp. 558–568, 2019, doi: 10.1161/ATVBAHA.119.310961.

[12] A. Bashier, A. Bin Hussain, E. Abdelgadir, F. Alawadi, H. Sabbour, and R. Chilton, "Consensus recommendations for management of patients with type 2 diabetes mellitus and cardiovascular diseases," *Diabetol. Metab. Syndr.*, vol. 11, no. 1, pp. 1–28, 2019, doi: 10.1186/s13098-019-0476-0.

[13] B. Zareini *et al.*, "Type 2 Diabetes Mellitus and Impact of Heart Failure on Prognosis Compared to Other Cardiovascular Diseases: A Nationwide Study," *Circ. Cardiovasc. Qual. Outcomes*, vol. 13, no. 7, pp. 386–394, 2020, doi: 10.1161/CIRCOUTCOMES.119.006260.

[14] T. Mueller, F. Hinterreiter, C. Luft, W. Poelz, M. Haltmayer, and B. Dieplinger, "Mortality rates and mortality predictors in patients with symptomatic peripheral artery disease stratified according to age and diabetes," *J. Vasc. Surg.*, vol. 59, no. 5, pp. 1291–1299, 2014, doi: 10.1016/j.jvs.2013.11.063.

[15] C. Höbaus, C. T. Herz, T. Wrba, R.

Koppensteiner, and G. H. Schernthaner, "Peripheral arterial disease and type 2 diabetes: Older patients still exhibit a survival benefit from glucose control," *Diabetes Vasc. Dis. Res.*, vol. 17, no. 2, 2020, doi: 10.1177/1479164120914845.

[16] O. B. Ajagbe, Z. Kabair, and T. O'Connor, "Survival analysis of adult tuberculosis disease," *PLoS One*, vol. 9, no. 11, 2014, doi: 10.1371/journal.pone.0112838.

[17] L. Brookman-Frazee *et al.*, "Using survival analysis to understand patterns of sustainment within a system-driven implementation of multiple evidence-based practices for children's mental health services," *Front. Public Heal.*, vol. 6, no. MAR, pp. 1–12, 2018, doi: 10.3389/fpubh.2018.00054.

[18] M. Nadjib Bustan, Arman, M. K. Aidid, F. A. Gobel, and Syamsidar, "Cox Proportional Hazard Survival Analysis on Inpatient Breast Cancer Cases," *J. Phys. Conf. Ser.*, vol. 1028, no. 1, 2018, doi: 10.1088/1742-6596/1028/1/012230.

[19] M. Kleinbaum, David G. Klein, *Survival Analysis. A self-A self-Learning text*. 2012.

[20] W. Sanusi, Alimuddin, and Sukmawati, "Model Regresi Cox dan Aplikasinya dalam Menganalisis Ketahanan Hidup Pasien Penderita Diabetes Mellitus di Rumah Sakit Bhayangkara Makassar," *J. Math. Comput. Stat.*, vol. 1, no. 1, pp. 62–77, 2018.

[21] A. B. Shaik, S. C. Thasleema, R. Nakkala, and M. Venkataramanaiah, "A Study on Type 2 Diabetes Mellitus Patients Using Regression Model and Survival Analysis Techniques," vol. 6, no. 1, pp. 514–522, 2018.

[22] I. A. P. R. DEWI, N. L. P. SUCIPTAWATI, and N. K. T. TASTRAWATI, "Aplikasi Regresi Cox Proportional Hazard Pada Sintasan Pasien Diabetes Melitus," *E-Jurnal Mat.*, vol. 7, no. 3, p. 278, 2018, doi: 10.24843/mtk.2018.v07.i03.p215.

[23] D. Irawan, "Prevalensi dan Faktor Risiko Kejadian Diabetes Melitus Tipe 2 di Daerah Urban Indonesia," *Univ. Indones.*, pp. 1–121, 2010.

[24] A. A. Putri and S. Astutik, "Survival Analysis On The Rate Of Diabetes Mellitus Patient Recovery With Bayesian Methode," vol. 8, no. 1, pp. 268–272, 2017.

[25] Mildawati, N. Diani, and A. Wahid, "Hubungan Usia, Jenis Kelamin dan Lama Menderita Diabetes dengan Kejadian Neuropati Perifer Diabateik," *Caring Nurs. J.*, vol. 3, no. 2, pp. 31–37, 2019.

[26] B. Derebew, "Survival Analysisof Recurrent Events: An Application To Diabetes Mellitus Patients In The Case Of Menellik Ii Referral Hospital," ADDIS ABABA UNIVERSITY, 2016.

[27] Kementrian Kesehatan Republik Indonesia, *Pedoman Pelayanan Kefarmasian Pada Diabetes Melitus*. Jakarta: Kementerian Kesehatan Republik Indonesia. Direktorat Jendera Kefarmasian dan Alat Kesehatanl, 2019.

[28] L. I. A. Anggraeni, "Hazard Pada Penderita Diabetes Melitus Tipe Ii Comparison Analysis Using Weibull Regression and Cox Proportional Hazard Regression of Patients

Diabetes Melitus Type Ii in Rsud Ngudi Waluyo Wlingi on 2013," 2015.

hasil cek_endang darmawan

ORIGINALITY REPORT

16%	9%	11%	4%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	theses.gla.ac.uk Internet Source	2%
2	A W Harahap, M S Nasution. "Comparison quality of life patients treated with insulin and oral hypoglycemic drugs", IOP Conference Series: Earth and Environmental Science, 2018 Publication	1%
3	Submitted to Universitas Negeri Semarang Student Paper	1%
4	theijes.com Internet Source	1%
5	repository.uma.ac.id Internet Source	1%
6	eprints.manipal.edu Internet Source	<1%
7	"Poster Session Clinical", European Journal of Heart Failure, 2013. Publication	<1%
8	Submitted to Ain Shams University Student Paper	<1%

9	John M. Clements, Brady T. West, Zachary Yaker, Breanna Lauinger et al. "Disparities in diabetes-related multiple chronic conditions and mortality: The influence of race", Diabetes Research and Clinical Practice, 2020 Publication	<1 %
10	Ravi Kant Upadhyay. "Emerging Risk Biomarkers in Cardiovascular Diseases and Disorders", Journal of Lipids, 2015 Publication	<1 %
11	"42nd EASD Annual Meeting of the European Association for the Study of Diabetes", Diabetologia, 2006 Publication	<1 %
12	jurnal.polibatam.ac.id Internet Source	<1 %
13	www.rroij.com Internet Source	<1 %
14	D. Dutta, V. Arora, A. Dhingra, A.K. Das et al. "Quinary prevention in diabetes care: Need for multidisciplinary approach", Clinical Epidemiology and Global Health, 2021 Publication	<1 %
15	Submitted to Udayana University Student Paper	<1 %
16	www.oncotarget.com Internet Source	

		<1%
17	Submitted to Mount Kenya University Student Paper	<1%
18	Ning Eliyati, Sri Indra Maiyanti, Oki Dwipurwani, Shaly Wanda Hamidah. "MODEL REGRESI COX UNTUK MENGANALISIS PENGARUH FAKTOR ASUPAN MAKANAN TERHADAP RISIKO KEKAMBUHAN ENDOMETRIOSIS", BAREKENG: Jurnal Ilmu Matematika dan Terapan, 2021 Publication	<1%
19	Coskun Durmus, Sertac Yetiser, Ozlem Durmus. "Auditory brainstem evoked responses in insulin-dependent (ID) and non-insulin-dependent (NID) diabetic subjects with normal hearing", International Journal of Audiology, 2009 Publication	<1%
20	Submitted to Middlesex University Student Paper	<1%
21	Nihar R. Desai, William H. Shrank, Michael A. Fischer, Jerry Avorn et al. "Patterns of Medication Initiation in Newly Diagnosed Diabetes Mellitus: Quality and Cost Implications", The American Journal of Medicine, 2012 Publication	<1%

22	clinmedjournals.org Internet Source	<1%
23	Juleen R. Zierath Harriet Wallberg-Henriksson,. "GLUT4: a key player regulating glucose homeostasis? Insights from transgenic and knockout mice", Molecular Membrane Biology, 2009 Publication	<1%
24	qdoc.tips Internet Source	<1%
25	www.citeulike.org Internet Source	<1%
26	www.hindawi.com Internet Source	<1%
27	Selam Tesfayohannes Amha, Sisay Moges, Sisay Shine, Abinet Dagnaw. "Survival Status and Its Predictors Among Adult Human Immunodeficiency Virus Infected Patients Attending Their Antiretroviral Treatment at Health Centers in Kirkos Sub City, Addis Ababa, Ethiopia. A Retrospective Cohort Study", Research Square, 2020 Publication	<1%
28	Andri Setyorini, Supriyadi Supriyadi. "Stress of Type 2 Diabetes Mellitus Patients in	<1%

Implementation Self Care Management", STRADA Jurnal Ilmiah Kesehatan, 2020
Publication

29	Submitted to Higher Education Commission Pakistan Student Paper	<1 %
30	Josefien van Olmen, Pilvikki Absetz, Roy William Mayega, Linda Timm et al. "The Process Evaluation of a Comparative Controlled Trial to Support Self-management for the Prevention and Management of Type 2 Diabetes in Uganda, South Africa and Sweden in the SMART2D Project.", Research Square Platform LLC, 2021 Publication	<1 %
31	www.kidney.org Internet Source	<1 %
32	Manu Goyal, Neil D. Reeves, Satyan Rajbhandari, Moi Hoon Yap. "Robust Methods for Real-Time Diabetic Foot Ulcer Detection and Localization on Mobile Devices", IEEE Journal of Biomedical and Health Informatics, 2019 Publication	<1 %
33	Qihuan Li, Mengyang Liu, Yingjie Zhang, Shangwu Wu et al. "The spatio-temporal analysis of the incidence of tuberculosis and the associated factors in mainland China,	<1 %

2009-2015", Infection, Genetics and Evolution, 2019
Publication

34	www.ojs.unm.ac.id Internet Source	<1 %
35	www.researchsquare.com Internet Source	<1 %
36	Artur Stolarczyk, Igor Jarzemski, Bartosz M. Maciąg, Magda Stolarczyk. "Balance and motion coordination parameters can be improved in patients with type 2 diabetes with physical balance training – non-randomized controlled trial", Research Square, 2020 Publication	<1 %
37	Fabbian, Fabio, Alfredo De Giorgi, Marcello Monesi, Marco Pala, Ruana Tiseo, Silvia Forcellini, Alda Storari, Roberto Graziani, Riccardo Volpi, Dimitri P. Mikhailidis, and Roberto Manfredini. "A possible relationship between renal impairment and complications development in type 2 diabetes mellitus: a prospective, observational study in Italy", Journal of Diabetes and its Complications, 2015. Publication	<1 %
38	Reizkiana Feva Kosmah Dewi, Meita Dhamayanti, Sri Endah Rahayuningsih, Kuswandewi Mutyara et al. "Cultural	<1 %

	Perceptions of Child Abuse in Terms of Parents Perspective a Qualitative Study in Indonesia", Research Square, 2019 Publication	
39	doaj.org Internet Source	<1 %
40	pubmed.ncbi.nlm.nih.gov Internet Source	<1 %
41	qed.econ.queensu.ca Internet Source	<1 %
42	revistanefrologia.com Internet Source	<1 %
43	zenodo.ups.edu.ec Internet Source	<1 %
44	Mahalul Azam, Rina Sulistiana, Arulita Ika Fibriana, Soesmeyka Savitri, Syed Mohamed Al Junid. "Prevalence of Mental Health Disorders among Elderly Diabetics and Associated Risk Factors in Indonesia", Cold Spring Harbor Laboratory, 2020 Publication	<1 %
45	repository.unair.ac.id Internet Source	<1 %
46	"Diabetes and Exercise", Springer Science and Business Media LLC, 2018 Publication	<1 %

47	www.ajmc.com Internet Source	<1%
48	Julia Hafner, Bernhard Zierfuss, Gerit-Holger Schernthaner, Ursula Schmidt-Erfurth. "From the eye into the foot?", Atherosclerosis, 2020 Publication	<1%
49	cardiab.biomedcentral.com Internet Source	<1%
50	escholarship.org Internet Source	<1%
51	www.x-mol.com Internet Source	<1%

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		