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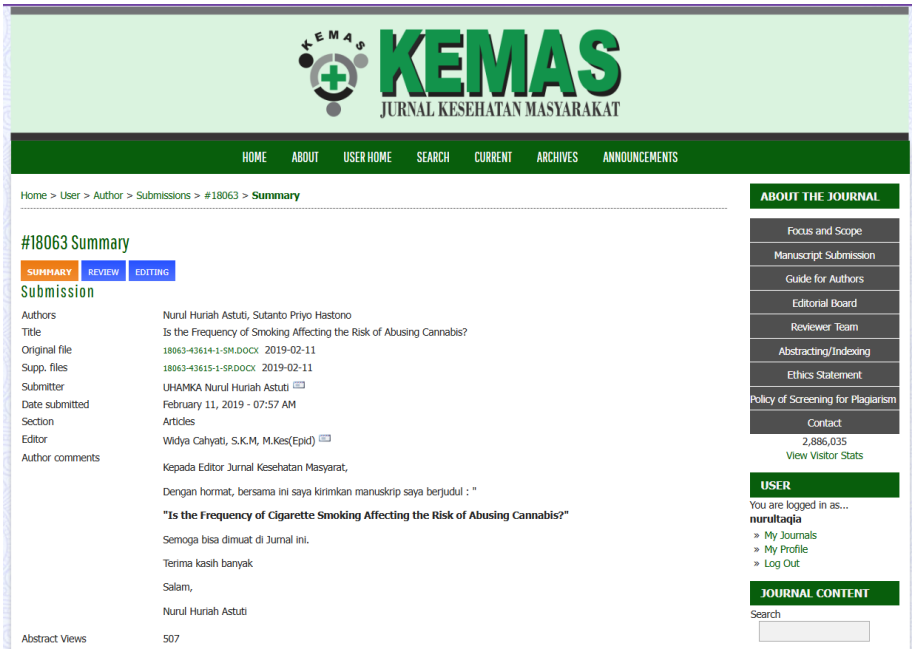

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#18063 Summary

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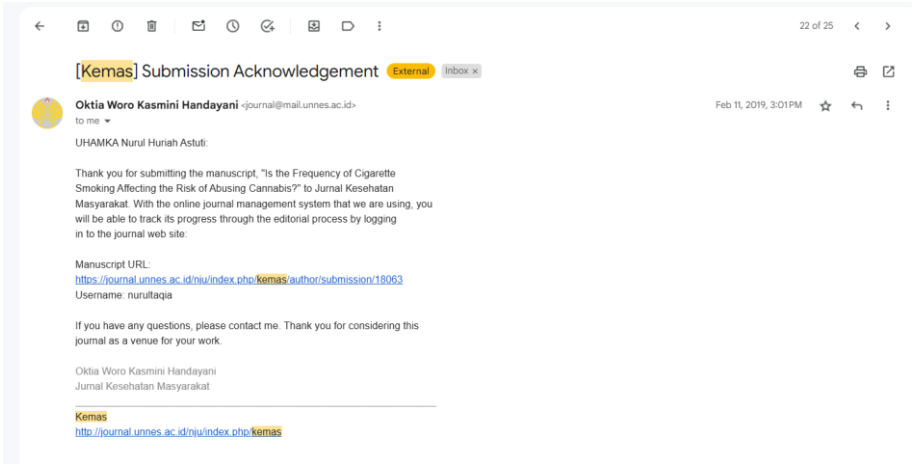

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Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. This study used secondary data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011. The results of this study found that durability or length of time for abusing cannabis was mostly 1-4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. The results of the life table analysis showed that the more cigarettes smoked, the more survival rate of abusing cannabis increased (based on five-year intervals). Multivariate analysis also showed that the more the number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders (history of drinking alcohol, families exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence). Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Preliminary

Indonesia is the third largest country in the world in terms of cigarette consumption (Report & Mpower, 2008). From the results of the Basic Health Research (Riskesdas) data analysis, it was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population. This number declined slightly in 2018, which was 28.8% of the population (Kementerian Kesehatan RI, 2018), However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 Indonesian people who cigatette smoke every day and every so often in 2013. Meanwhile according to the Basic Health Research (Riskesdas) in 2018, that number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million.

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Mayet, Aurelie, 2011). Speaking of theory, it is known

that there are three theories related to the relationship of smoking with cannabis abuse. First theory is “the Gateway Theory” (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the “choice” of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of “Route of Administration Model” (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia dan Pusat Penelitian Kesehatan Universitas Indonesia, 2012). Cannabis was also a drug type that had ever been used and for the last year was used by Indonesian students surveyed by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). In the meantime, the results of a descriptive analysis of three national surveys on the development of illicit drug abuse and circulation in student groups in Indonesia for three consecutive times (2006, 2009 and 2011) showed that the number of cigarette smokers in respondents reached 19% (in 2006 and 2009) and 20% in 2011. In particular, cigarette smoking rates for students who abuse drugs from the three surveys were 69%, 62%, and 52%. There was almost no difference of the cigarette smoking rate among the three surveys for those who were not abusers. The range was 16-17%. In other words, based on those three surveys, students who abuse drugs are three to four times more from those who cigarette smoke than non-abusers (Indonesia National Narcotics Agency and the Health Research Center of Indonesia University, 2012). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the

majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 – 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each hazard ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 – 2.56) and 3.49 (95% CI. 3.18 – 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

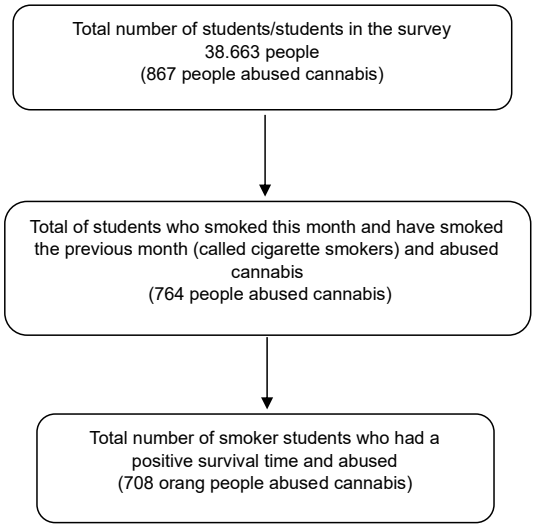


Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the strength of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week,> 7 – 35 cigarettes/week,> 35 – 70 cigarettes/week,> 70 – 140 cigarettes/week, and> 140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week,> 7 – 35 cigarettes/week, and> 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

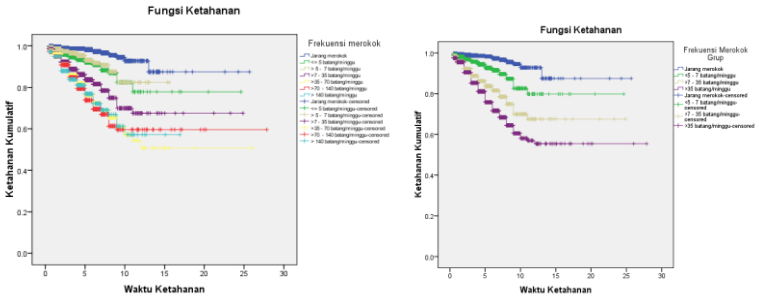


Figure 1. Comparison of Variable Groups Distribution in the Frequency of Smoking Based on the Kaplan Meier Curve

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 – 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Whereas talking about the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years, (Mayet, Aurelie, 2011).

Correlation between the First Time Age of Smoking to the First Time Age of Abusing Cannabis

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). And cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 – 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 – 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 – 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

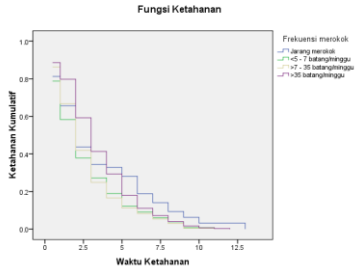
The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Kandel, 1975 in (Mayet, Aurelie, 2011)). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people

start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *ρ*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			



Graph 2. Kaplan Meier Curve of Student Smokers that Misused Cannabis Based on the Frequency of Smoking

Survival Rate of Abusing Cannabis Based on the Frequency of Cigarette Smoking

The results of life table analysis showed that at intervals of 0 – 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarelycigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking <5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking> 7 – 35 cigarettes/week was 0.85, and the group with a frequency> 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 3).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life – based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigareatte smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 3. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

Frequency of Smoking and Risk of Cannabis Abuse

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 4).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 4). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 – 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family

exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 – 3,3).

2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 – 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 – 5.3).
3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 – 6.0).

Table 4. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	***Pvalue***	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea Prince, 2011). Other studies also revealed that the history of drinking alcohol by someone also

increased the risk of experiencing drug abuse (Clark, Duncan, 2005; Dierke, Lisa C, 2007; Rose John, D, 2006). The second confounder in the correlation between the frequency of cigarette smoking and 14annabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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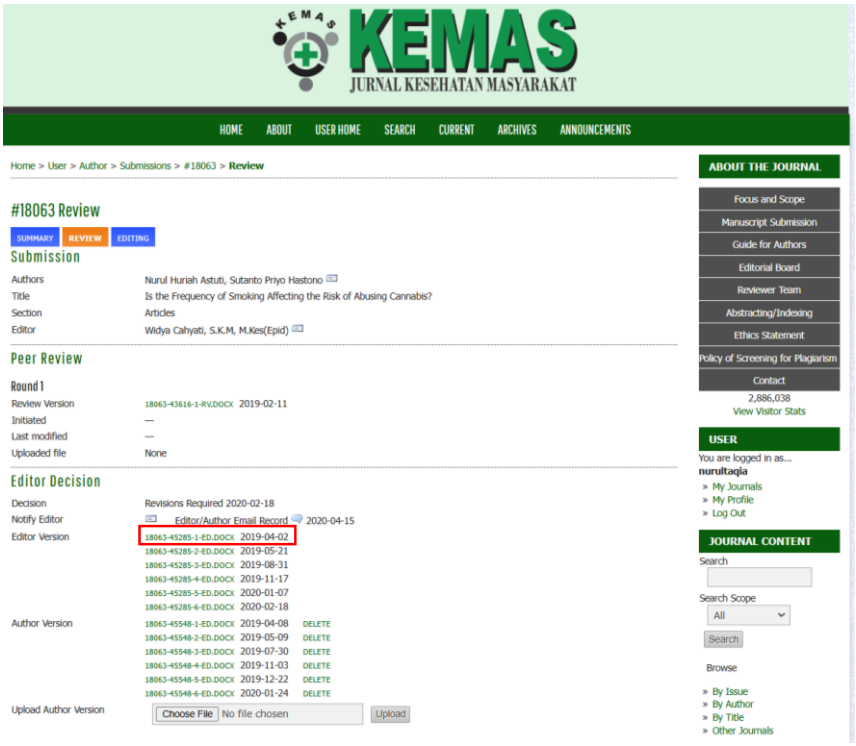

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#18063 Review

SUMMARY REVIEW EDITING

Submission

Authors	Nurul Huriah Astuti, Sutanto Priyo Hastono
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Section	Articles
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Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. This study used secondary data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011. The results of this study found that durability or length of time for abusing cannabis was mostly 1-4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. The results of the life table analysis showed that the more cigarettes smoked, the more survival rate of abusing cannabis increased (based on five-year intervals). Multivariate analysis also showed that the more the number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders (history of drinking alcohol, families exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence). Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

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Keywords: teens smokers, cannabis abuse, survival analysis

Preliminary

Indonesia is the third largest country in the world in terms of cigarette consumption (Report & Mpower, 2008). From the results of the Basic Health Research (Riskesdas) data analysis, it was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population. This number declined slightly in 2018, which was 28.8% of the population (Kementerian Kesehatan RI, 2018), However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 Indonesian people who cigatette smoke every day and every so often in 2013. Meanwhile according to the Basic Health Research (Riskesdas) in 2018, that number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million.

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Mayet, Aurelie, 2011). Speaking of theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia dan Pusat Penelitian Kesehatan Universitas Indonesia, 2012). Cannabis was also a drug type that had ever been used and for the last year was used by Indonesian students surveyed by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). In the meantime, the results of a descriptive analysis of three national surveys on the development of illicit drug abuse and circulation in student groups in Indonesia for three consecutive times (2006, 2009 and 2011) showed that the number of cigarette smokers in respondents reached 19% (in 2006 and 2009) and 20% in 2011. In particular, cigarette smoking rates for students who abuse drugs from the three surveys were

69%, 62%, and 52%. There was almost no difference of the cigarette smoking rate among the three surveys for those who were not abusers. The range was 16-17%. In other words, based on those three surveys, students who abuse drugs are three to four times more from those who cigarette smoke than non-abusers (Indonesia National Narcotics Agency and the Health Research Center of Indonesia University, 2012). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 – 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each hazard ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 – 2.56) and 3.49 (95% CI. 3.18 – 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

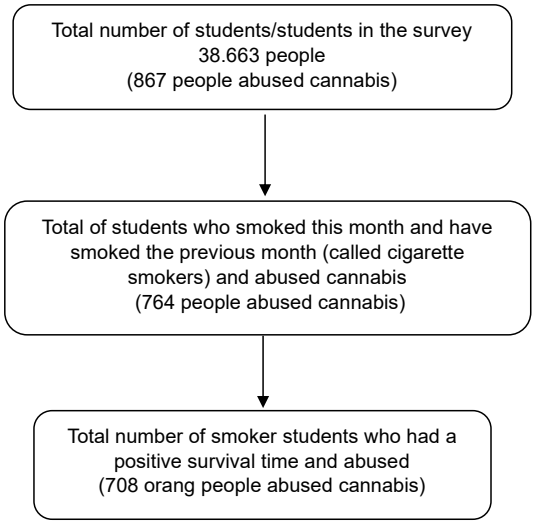

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the strength of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes

to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week,> 7 – 35 cigarettes/week,> 35 – 70 cigarettes/week,> 70 – 140 cigarettes/week, and> 140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week,> 7 – 35 cigarettes/week, and> 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

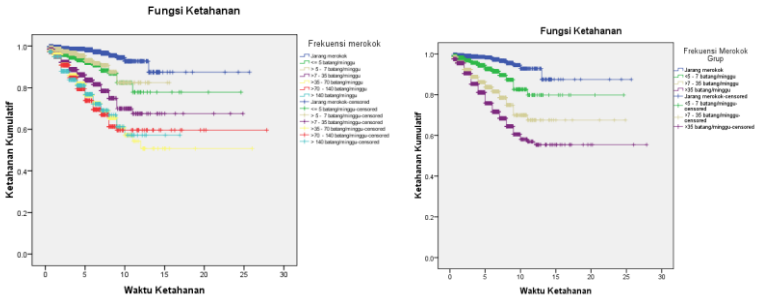

Figure 1. Comparison of Variable Groups Distribution in the Frequency of Smoking Based on the Kaplan Meier Curve

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Results and Discussion

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The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 – 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Whereas talking about the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years, (Mayet, Aurelie, 2011).

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained

from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). And cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 – 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 – 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 – 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

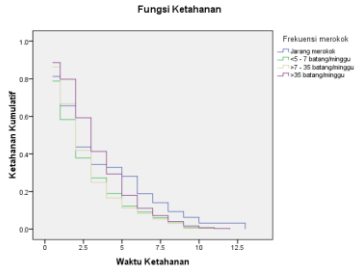
The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Kandel, 1975 in (Mayet, Aurelie, 2011)). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the

results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/weel	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			



Graph 2. Kaplan Meier Curve of Student Smokers that Misused Cannabis Based on the Frequency of Smoking

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The results of life table analysis showed that at intervals of 0 – 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarelycigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking <5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking> 7 – 35 cigarettes/week was 0.85, and the group with a frequency> 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 3).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life – based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigareatte

smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 3. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the 28annabis28 of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and

peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 4).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 4). Overall, the final model explains:

4. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 – 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 – 3,3).
5. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 – 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 – 5.3).
6. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 – 6.0).

Table 4. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	***Pvalue***	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**

Variable		B	SE	*Pvalue*	HR	95% CI
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea Prince, 2011). Other studies also revealed that the history of drinking alcohol by someone also increased the risk of experiencing drug abuse (Clark, Duncan, 2005; Dierke, Lisa C, 2007; Rose John, D, 2006). The second confounder in the correlation between the frequency of cigarette smoking and 30annabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of

committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

Acknowledgement

Researchers expressed their gratitude to the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) for their permission to process data on the National Survey on the Development of Drug Abuse and Circulation in Student Groups in Indonesia in 2011.

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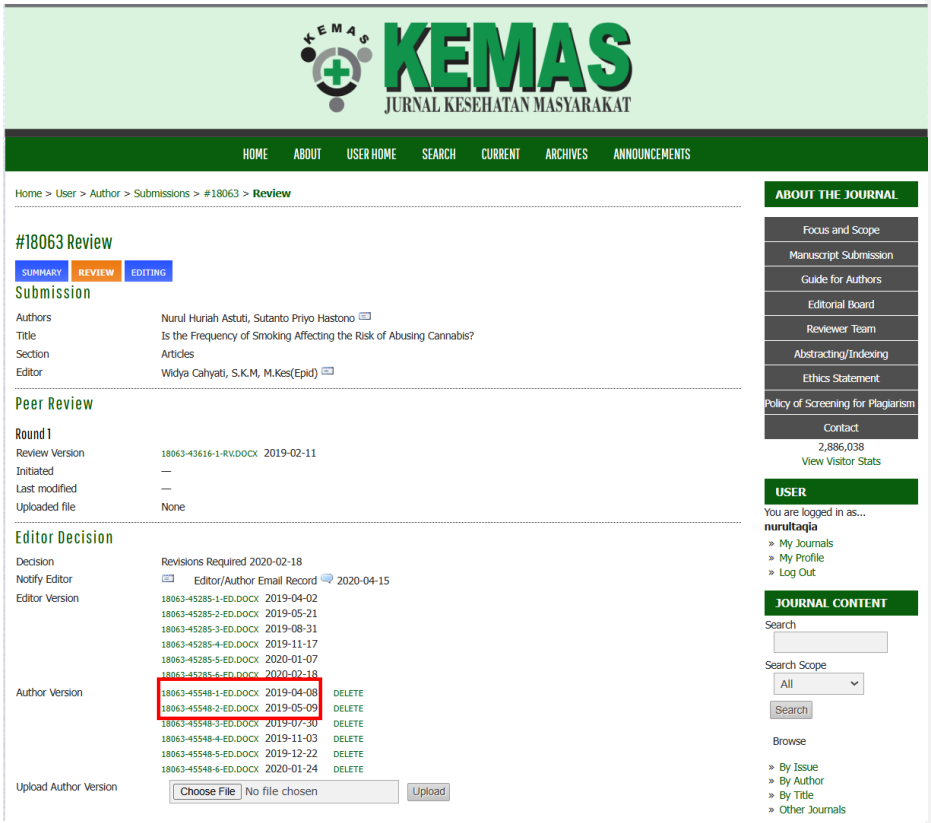
3. **Pengiriman revisi pertama (8 April 2019 dan 9 Mei 2019)**

(Pengiriman revisi 8 April dan 9 Mei 2019 isi revisi artikel sama, Penulis *double* mengirimkan)



Artikel yang telah direvisi pertama

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. The life table analysis showed that the more cigarettes smoked, the more survival rate of abusing cannabis increased (based on five-year intervals). Multivariate analysis also showed that the more the number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Onclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

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Introduction

Indonesia is the third largest country in the world in terms of cigarette consumption (Report & Mpower, 2008). From the results of the Basic Health Research (Riskesdas) data analysis, it was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population. This number declined slightly in 2018, which was 28.8% of the population (Kementerian Kesehatan RI, 2018), However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 Indonesian people who cigatette smoke every day and every so often in 2013. Meanwhile according to the Basic Health Research (Riskesdas) in 2018, that number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million.

Smoking habits are known to be the main cause of lung disease. Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Indraswari, Putu Ika Indah, et al, 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers. A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah, Kresnowati, & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Mayet, Aurelie, 2011). Speaking of theory, it is known

that there are three theories related to the relationship of smoking with cannabis abuse. First theory is “the Gateway Theory” (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the “choice” of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of “Route of Administration Model” (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia dan Pusat Penelitian Kesehatan Universitas Indonesia, 2012). Cannabis was also a drug type that had ever been used and for the last year was used by Indonesian students surveyed by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). In the meantime, the results of a descriptive analysis of three national surveys on the development of illicit drug abuse and circulation in student groups in Indonesia for three consecutive times (2006, 2009 and 2011) showed that the number of cigarette smokers in respondents reached 19% (in 2006 and 2009) and 20% in 2011. In particular, cigarette smoking rates for students who abuse drugs from the three surveys were 69%, 62%, and 52%. There was almost no difference of the cigarette smoking rate among the three surveys for those who were not abusers. The range was 16-17%. In other words, based on those three surveys, students who abuse drugs are three to four times more from those who cigarette smoke than non-abusers (Indonesia National Narcotics Agency and the Health Research Center of Indonesia University, 2012). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the

majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

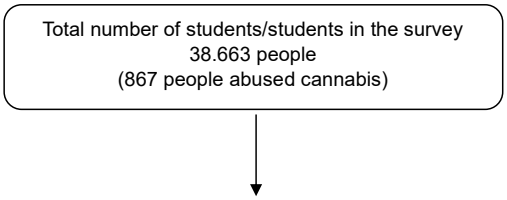
Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 – 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each hazard ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 – 2.56) and 3.49 (95% CI. 3.18 – 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).



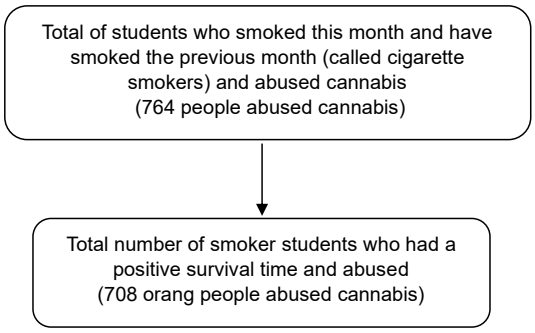


Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the strength of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week,> 7 – 35 cigarettes/week,> 35 – 70 cigarettes/week,> 70 – 140 cigarettes/week, and> 140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week,> 7 – 35 cigarettes/week, and> 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

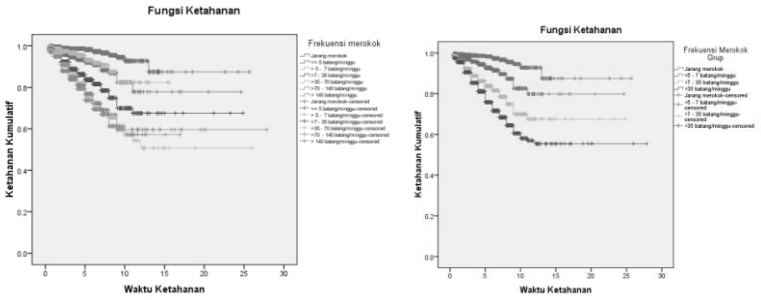


Figure 1. Comparison of Variable Groups Distribution in the Frequency of Smoking Based on the Kaplan Meier Curve

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Results and Discussion

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The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 – 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
	1 – 4 years	435	61.5

Variable		Total N = 708	Percentage (%)
Length of time/survival time from smoking to misusing cannabis	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Whereas talking about the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years, (Mayet, Aurelie, 2011).

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *p*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). And cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 – 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 – 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 – 2.2).

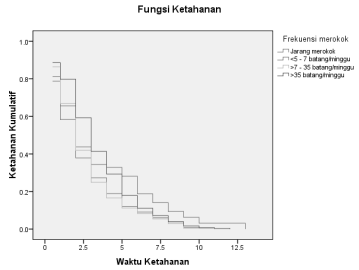
The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Kandel, 1975 in (Mayet, Aurelie, 2011)). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette

smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 2. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			



Graph 2. Kaplan Meier Curve of Student Smokers that Misused Cannabis Based on the Frequency of Smoking

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The results of life table analysis showed that at intervals of 0 – 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarelycigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking <5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking> 7 – 35 cigarettes/week was 0.85, and the group with a frequency> 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 3).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life – based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigareatte smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 3. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 4).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 4). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 – 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol,

family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 – 3,3).

2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 – 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 – 5.3).
3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 – 6.0).

Table 4. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	***Pvalue***	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea

Prince, 2011). Other studies also revealed that the history of drinking alcohol by someone also increased the risk of experiencing drug abuse (Clark, Duncan, 2005; Dierke, Lisa C, 2007; Rose John, D, 2006). The second confounder in the correlation between the frequency of cigarette smoking and 45annabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

Acknowledgement

Researchers expressed their gratitude to the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) for their permission to process data on the National Survey on the Development of Drug Abuse and Circulation in Student Groups in Indonesia in 2011.

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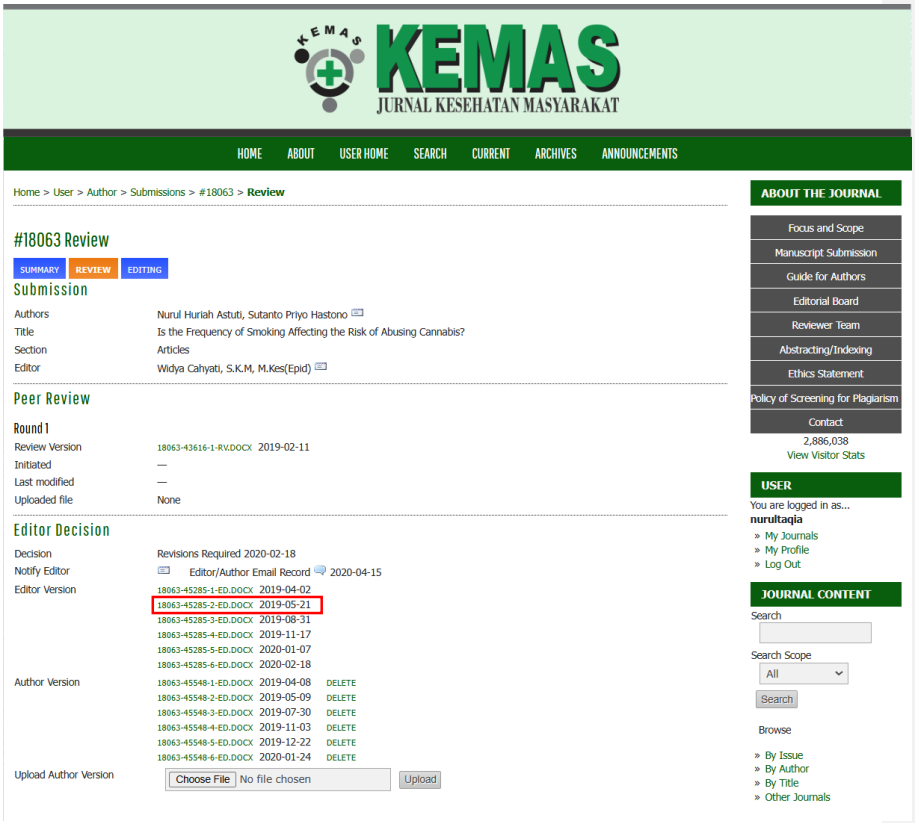

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival

analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. The life table analysis showed that the more cigarettes smoked, the more survival rate of abusing cannabis increased (based on five-year intervals). Multivariate analysis also showed that the more the number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Indonesia is the third largest country in the world in terms of cigarette consumption (Report & Mpower, 2008). From the results of the Basic Health Research (Riskesdas) data analysis, it was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population. This number declined slightly in 2018, which was 28.8% of the population (Kementerian Kesehatan RI, 2018), However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 Indonesian people who cigatette smoke every day and every so often in 2013. Meanwhile according to the Basic Health Research (Riskesdas) in 2018, that number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million.

Smoking habits are known to be the main cause of lung disease. Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Indraswari, Putu Ika Indah, et al, 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers. A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah, Kresnowati, & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Mayet, Aurelie, 2011). Speaking of theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to

illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia dan Pusat Penelitian Kesehatan Universitas Indonesia, 2012). Cannabis was also a drug type that had ever been used and for the last year was used by Indonesian students surveyed by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). In the meantime, the results of a descriptive analysis of three national surveys on the development of illicit drug abuse and circulation in student groups in Indonesia for three consecutive times (2006, 2009 and 2011) showed that the number of cigarette smokers in respondents reached 19% (in 2006 and 2009) and 20% in 2011. In particular, cigarette smoking rates for students who abuse drugs from the three surveys were 69%, 62%, and 52%. There was almost no difference of the cigarette smoking rate among the three surveys for those who were not abusers. The range was 16-17%. In other words, based on those three surveys, students who abuse drugs are three to four times more from those who cigarette smoke than non-abusers (Indonesia National Narcotics Agency and the Health Research Center of Indonesia University, 2012). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 – 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each hazard ratio/HR

(the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 – 2.56) and 3.49 (95% CI. 3.18 – 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

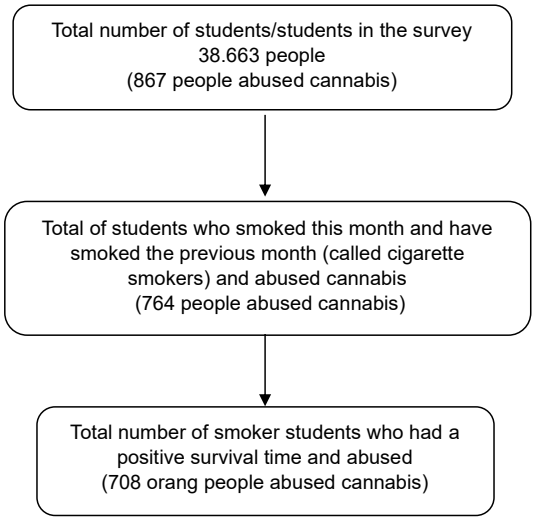

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the strength of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week,> 7 – 35 cigarettes/week,> 35 – 70 cigarettes/week,> 70 – 140 cigarettes/week, and> 140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week,> 7 – 35 cigarettes/week, and> 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

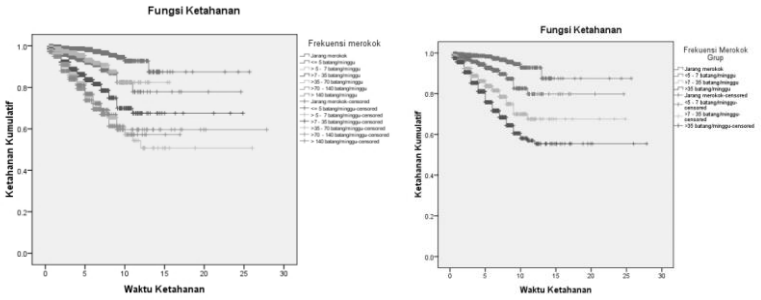

Figure 1. Comparison of Variable Groups Distribution in the Frequency of Smoking Based on the Kaplan Meier Curve

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Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 – 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
	1 – 4 years	435	61.5

Variable		Total N = 708	Percentage (%)
Length of time/survival time from smoking to misusing cannabis	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Whereas talking about the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years, (Mayet, Aurelie, 2011).

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *p*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). And cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 – 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 – 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 – 2.2).

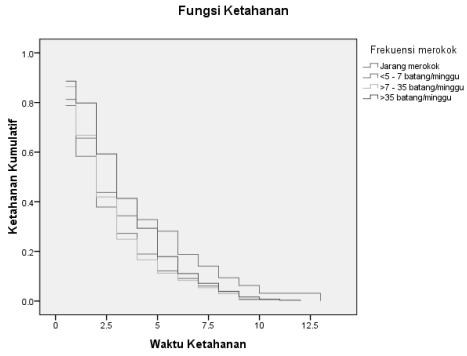
The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Kandel, 1975 in (Mayet, Aurelie, 2011)). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette

smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 2. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			



Graph 2. Kaplan Meier Curve of Student Smokers that Misused Cannabis Based on the Frequency of Smoking

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The results of life table analysis showed that at intervals of 0 – 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarelycigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking <5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking> 7 – 35 cigarettes/week was 0.85, and the group with a frequency> 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 3).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life – based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigareatte smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 3. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 4).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 4). Overall, the final model explains:

7. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 – 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family

exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 – 3,3).

8. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 – 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 – 5.3).
9. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 – 6.0).

Table 4. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	***Pvalue***	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea

Prince, 2011). Other studies also revealed that the history of drinking alcohol by someone also increased the risk of experiencing drug abuse (Clark, Duncan, 2005; Dierke, Lisa C, 2007; Rose John, D, 2006). The second confounder in the correlation between the frequency of cigarette smoking and 59annabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

Acknowledgement

Researchers expressed their gratitude to the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) for their permission to process data on the National Survey on the Development of Drug Abuse and Circulation in Student Groups in Indonesia in 2011.

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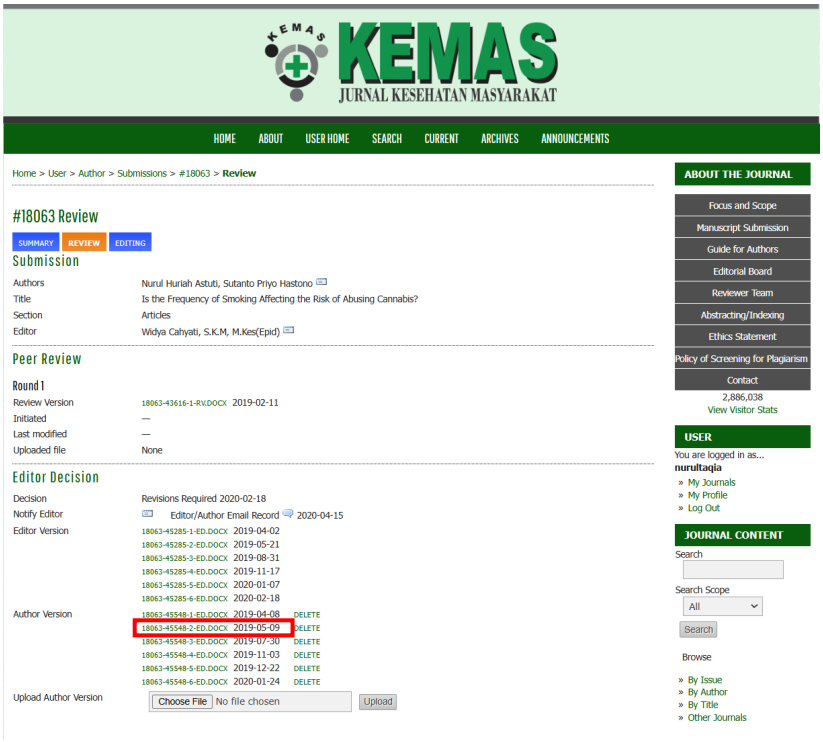

Artikel yang telah direvisi kedua

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

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The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was mostly 1-4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Preliminary

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Hindocha et al., 2015; Mayet, Aurelie, 2011). Speaking of theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is “the Gateway Theory” (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Lynskey & Agrawal, 2018; Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the “choice” of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of “Route of Administration Model” (ROM) which states that the techniques

of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 – 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each hazard ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 – 2.56) and 3.49 (95% CI. 3.18 – 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

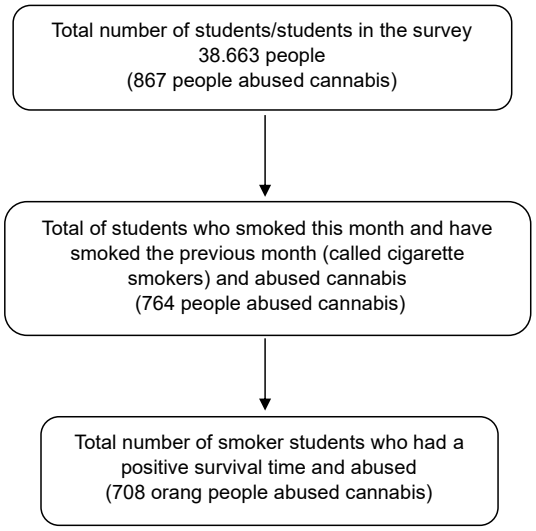

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the strength of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week,> 7 – 35 cigarettes/week,> 35 – 70

cigarettes/week,> 70 – 140 cigarettes/week, and> 140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week,> 7 – 35 cigarettes/week, and> 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

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The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 – 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Whereas talking about the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly

differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years, (Mayet, Aurelie).

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *p*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 – 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 – 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 – 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Kandel, 1975 in Mayet, Aurelie, 2011; Weinberger et al., 2018; Kristman-valente et al., 2017; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the

opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 – 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarelycigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking <5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking> 7 – 35 cigarettes/week was 0.85,

and the group with a frequency> 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life – based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 – 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 – 3,3).
2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 – 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 – 5.3).
3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 – 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**Pvalue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0

Variable		B	SE	Pvalue	HR	95% CI
Exposed Families						
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea Prince, 2011). The second confounder in the correlation between the frequency of cigarette smoking and 71annabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six

months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

Acknowledgement

Researchers expressed their gratitude to the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) for their permission to process data on the National Survey on the Development of Drug Abuse and Circulation in Student Groups in Indonesia in 2011.

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6. Menerima tanggapan dari Jurnal KEMAS untuk revisi ketiga (31 Agustus 2019)

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was mostly 1-4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Preliminary

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Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Hindocha et al., 2015; Mayet, Aurelie, 2011). Speaking of theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is “the Gateway Theory” (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances,

such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Lynskey & Agrawal, 2018; Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 – 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each hazard ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 – 2.56) and 3.49 (95% CI. 3.18 – 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis.

Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

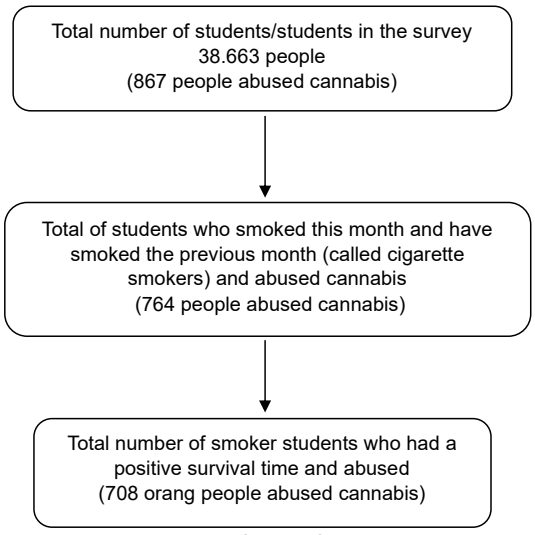

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the strength of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 – 35 cigarettes/week, >35 – 70 cigarettes/week, >70 – 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 – 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 – 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4

Variable		Total N = 708	Percentage (%)
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Whereas talking about the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years, (Mayet, Aurelie).

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 – 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 – 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 – 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Kandel, 1975 in Mayet, Aurelie, 2011; Weinberger et al., 2018; Kristman-valente et al., 2017; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5

<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 – 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarelycigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking <5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking> 7 – 35 cigarettes/week was 0.85, and the group with a frequency> 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life – based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 – 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 – 3,3).
2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 – 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 – 5.3).

3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 – 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**Pvalue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea Prince, 2011). The second confounder in the correlation between the frequency of cigarette smoking and 83annabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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Researchers expressed their gratitude to the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI) for their permission to process data on the National Survey on the Development of Drug Abuse and Circulation in Student Groups in Indonesia in 2011.

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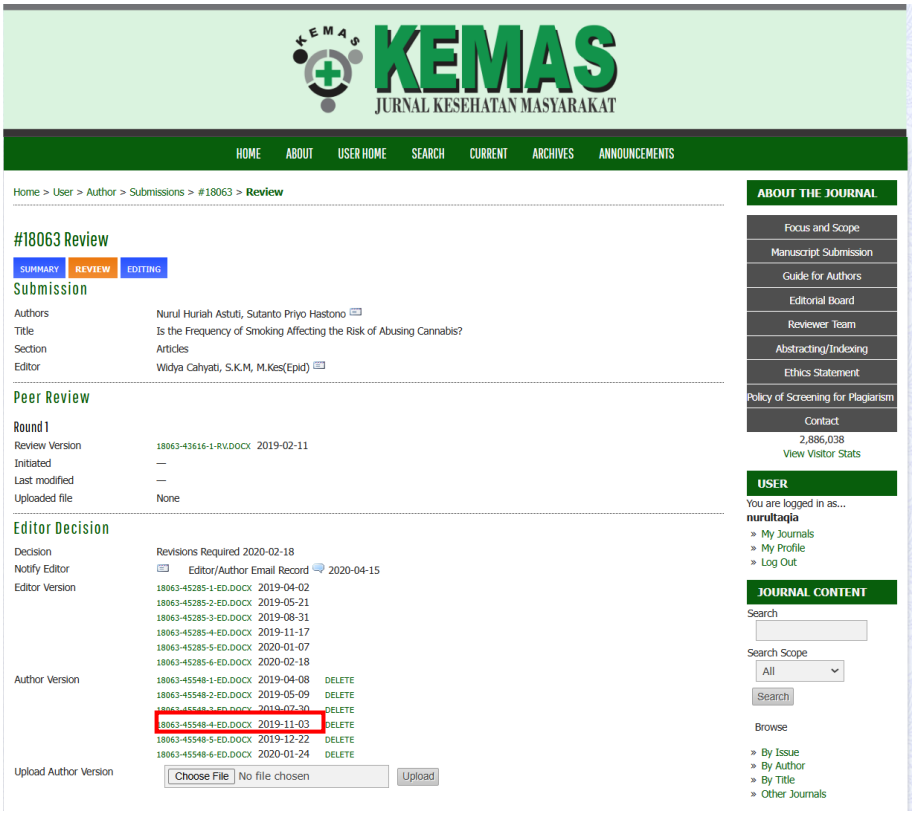

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was

mostly 1 – 4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Smoking habits are known to be the main cause of lung disease. Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Indraswari, Putu Ika Indah, et al, 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers. A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah, Kresnowati, & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Hindocha et al., 2015; Mayet, Aurelie, 2011). Based on the theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and

then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

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Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 - 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each Hazard Ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 - 2.56) and 3.49 (95% CI. 3.18 - 3.83) (Agrawal, Arpana, 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis

abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

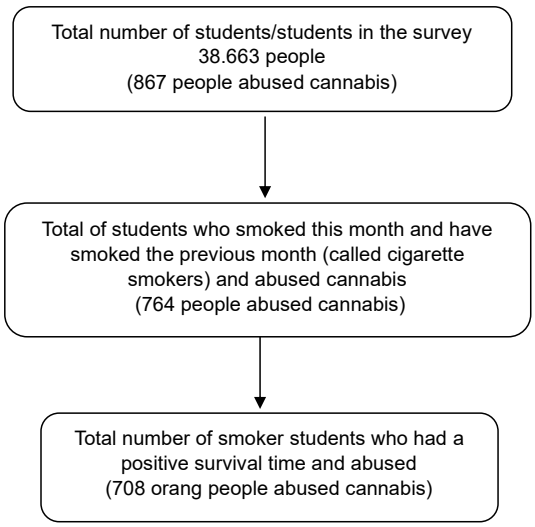

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the Power of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 - 35 cigarettes/week, >35 - 70 cigarettes/week, >70 - 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 - 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 - 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4

Variable		Total N = 708	Percentage (%)
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Regarding the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years (Mayet, Aurelie, 2011)

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 - 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 - 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 - 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Weinberger et al., 2018; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *ρ*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3

>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 - 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarely cigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking < 5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking > 7 – 35 cigarettes/week was 0.85, and the group with a frequency > 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life - based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 - 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 - 3,3).
2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 - 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 - 5.3).
3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia

in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 - 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**PValue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea Prince, 2011). The second confounder in the correlation between the frequency of cigarette smoking and canabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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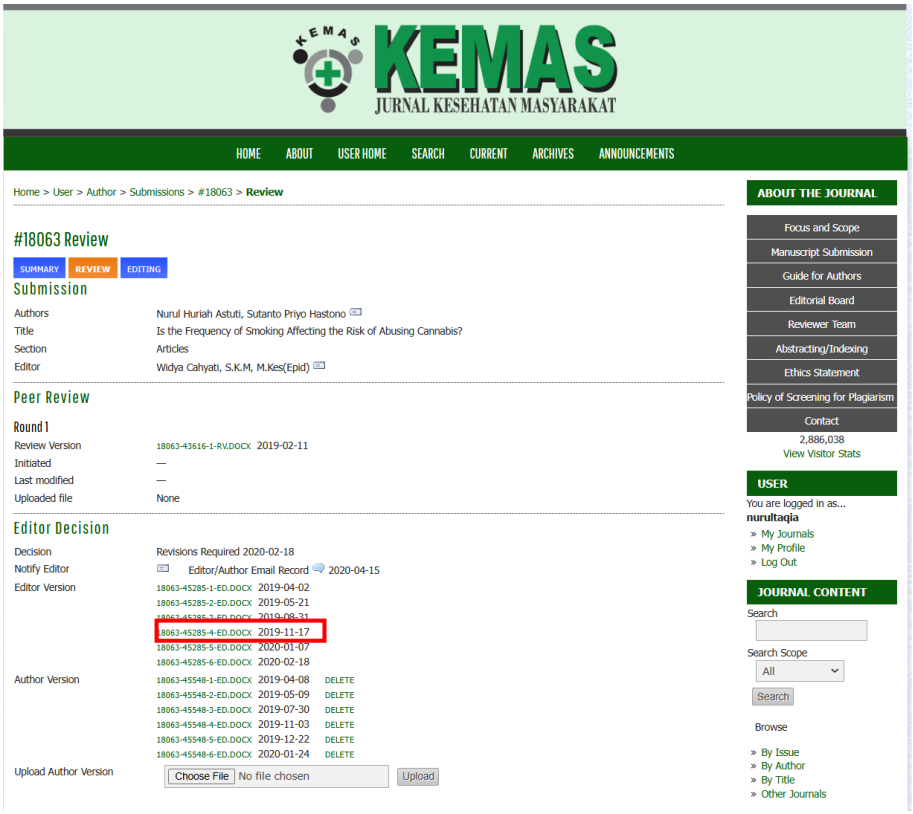
8. Menerima tanggapan dari jurnal KEMAS untuk revisi keempat (17 November 2019)



Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival

analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was mostly 1 – 4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Smoking habits are known to be the main cause of lung disease. Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Indraswari, Putu Ika Indah, et al, 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers. A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah, Kresnowati, & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Hindocha et al., 2015; Mayet, Aurelie, 2011). Based on the theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is

predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Van Leeuwen, Andrea Prince, 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhornen, Tellervo, 2008; Van Leeuwen, Andrea Prince, 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Van Leeuwen, Andrea Prince, 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet, Aurelie, 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 - 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each Hazard Ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 - 2.56) and 3.49 (95% CI. 3.18 - 3.83) (Agrawal, Arpana, 2013).

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Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

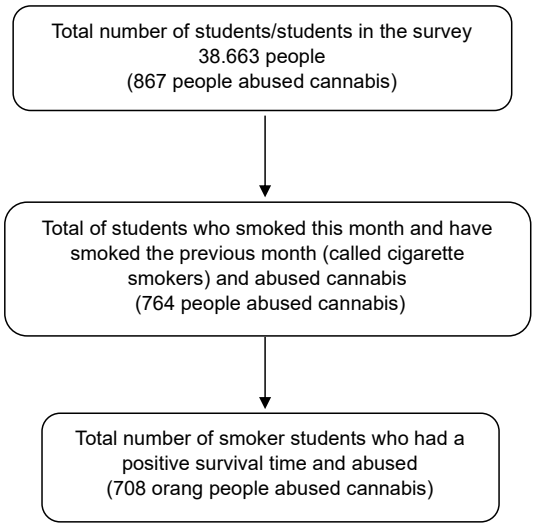

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal, Arpana, 2013). Then the Power of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 - 35 cigarettes/week, >35 - 70 cigarettes/week, >70 - 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 - 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve (Graph 1). The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet, Aurelie, 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 - 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4

Variable		Total N = 708	Percentage (%)
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Regarding the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years (Mayet, Aurelie, 2011)

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Van Leeuwen, Andrea Prince, 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhornen, Tellervo, 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 - 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 - 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 - 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens, et al, 2007 in (Mayet, Aurelie, 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Weinberger et al., 2018; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen, Andrea Prince, 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet, Aurelie, 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4

>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 - 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarely cigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking < 5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking > 7 – 35 cigarettes/week was 0.85, and the group with a frequency > 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life - based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal, Arpana, 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal, Arpana, 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

10. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 - 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 - 3,3).

11. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 - 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 - 5.3).
12. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 - 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**PValue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Van Leeuwen, Andrea Prince, 2011). The second confounder in the correlation between the frequency of cigarette smoking and canabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common

Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Van Leeuwen, Andrea Prince, 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen, Tellervo, 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen, Tellervo, 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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9. Pengiriman revisi artikel keempat (22 November 2020)

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was mostly 1 – 4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Smoking habits are known to be the main cause of lung disease. Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Indraswari et al., 2018). Smoking habits not only

cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers. A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Hindocha et al., 2015; Mayet et al., 2011). Based on the theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Prince van Leeuwen et al., 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhonen et al., 2008; Prince van Leeuwen et al., 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Prince van Leeuwen et al., 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet et al., 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 - 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each Hazard Ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 - 2.56) and 3.49 (95% CI. 3.18 - 3.83) (Agrawal et al., 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

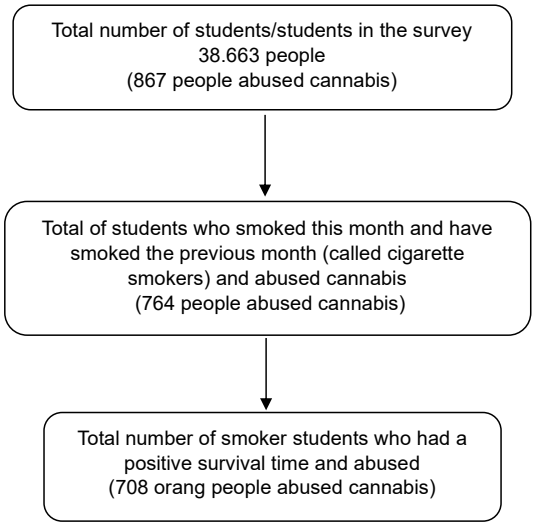

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal et al., 2013). Then the Power of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 - 35 cigarettes/week, >35 - 70 cigarettes/week, >70 - 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 - 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet et al., 2011).

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	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Regarding the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years (Mayet et al., 2011)

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could

be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Prince van Leeuwen et al., 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhonen et al., 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 - 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 - 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 - 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens et al, 2007 in (Mayet et al., 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Weinberger et al., 2018; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen et al., 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet et al., 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *ρ*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 - 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarely cigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking < 5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking > 7 – 35 cigarettes/week was 0.85, and the group with a frequency > 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers

could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life - based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal et al., 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal et al., 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were

confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 - 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 - 3,3).
2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 - 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 - 5.3).
3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 - 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**PValue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7

Variable		B	SE	PValue	HR	95% CI
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Prince van Leeuwen et al., 2011). The second confounder in the correlation between the frequency of cigarette smoking and canabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Prince van Leeuwen et al., 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhonen et al., 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhonen et al., 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and

cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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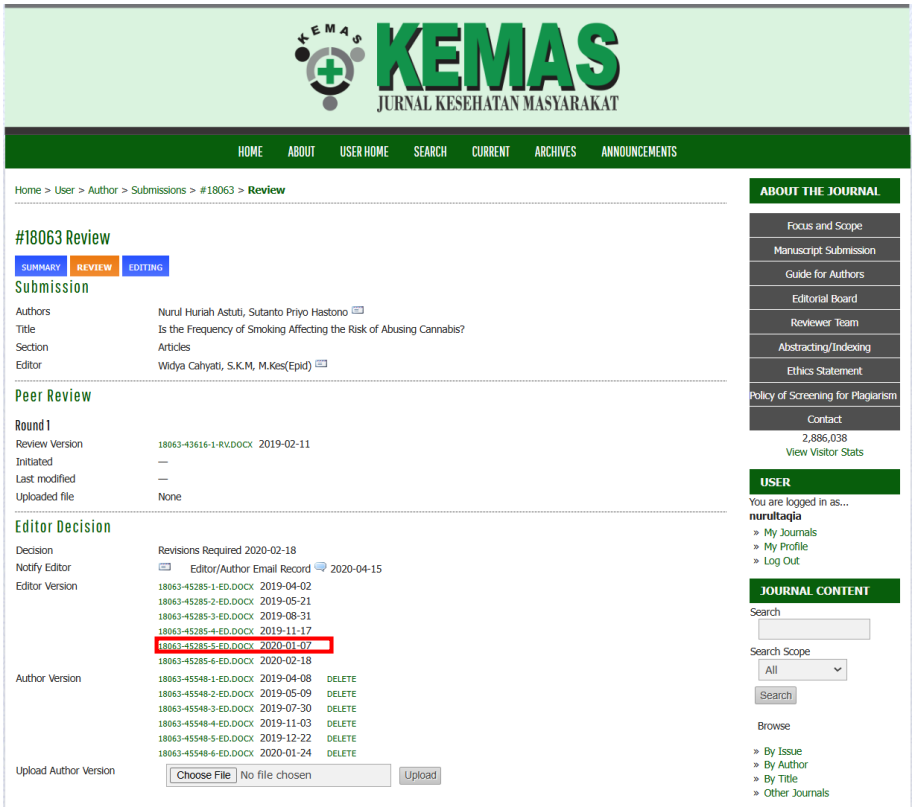
10. Menerima tanggapan dari jurnal KEMAS untuk revisi kelima



Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was

mostly 1 – 4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Smoking habits are known to be the main cause of lung disease. Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Indraswari et al., 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers. A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Hindocha et al., 2015; Mayet et al., 2011). Based on the theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by

consuming prohibited types of hard drugs, such as cocaine or heroin (Prince van Leeuwen et al., 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhonen et al., 2008; Prince van Leeuwen et al., 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Prince van Leeuwen et al., 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet et al., 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 - 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each Hazard Ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 - 2.56) and 3.49 (95% CI. 3.18 - 3.83) (Agrawal et al., 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis

abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

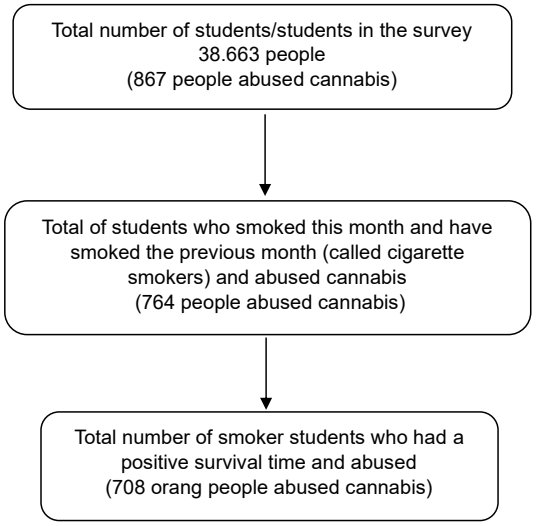

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal et al., 2013). Then the Power of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 - 35 cigarettes/week, >35 - 70 cigarettes/week, >70 - 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 - 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet et al., 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 - 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6

Variable		Total N = 708	Percentage (%)
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Regarding the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years (Mayet et al., 2011)

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Prince van Leeuwen et al., 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhonen et al., 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 - 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 - 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 - 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens et al, 2007 in (Mayet et al., 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Weinberger et al., 2018; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen et al., 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet et al., 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *ρ*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 - 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarely cigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking < 5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking > 7 – 35 cigarettes/week was 0.85, and the group with a frequency > 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life - based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal et al., 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal et al., 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

1. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 - 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 - 3,3).

2. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 - 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 - 5.3).
3. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 - 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**PValue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Prince van Leeuwen et al., 2011). The second confounder in the correlation between the frequency of cigarette smoking and canabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common

Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Prince van Leeuwen et al., 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhonen et al., 2008).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research shows that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhonen et al., 2008).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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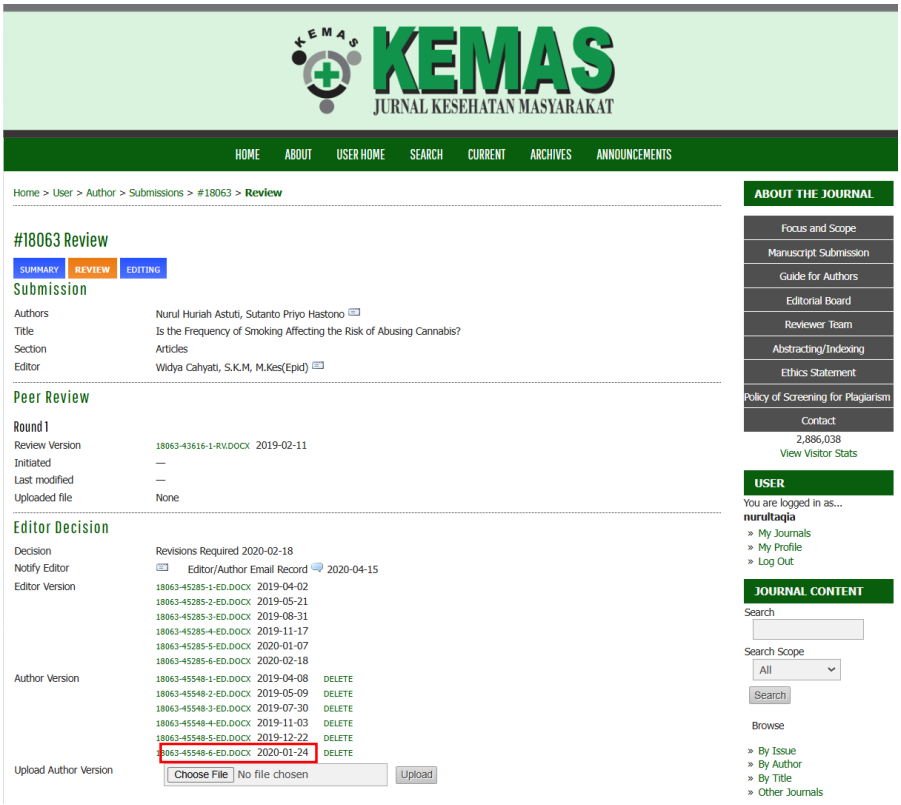

Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was

mostly 1 – 4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Smoking habits are known to be the main cause of lung disease, like chronic obstructive pulmonary disease (Diaz-Guzman & Mannino, 2014). Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Gates et al., 2014; Indraswari et al., 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers (Öberg, et al., 2011). A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah & Mufid, 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Badiani et al., 2015; Hindocha et al., 2015; Mayet, Aurelie, 2011). Based on the theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming

cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs, such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Secades-Villa et al., 2015; Prince van Leeuwen et al., 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhonen et al., 2008; Prince van Leeuwen et al., 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Prince van Leeuwen et al., 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet et al., 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 - 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each Hazard Ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 - 2.56) and 3.49 (95% CI. 3.18 - 3.83) (Agrawal et al., 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking.

Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

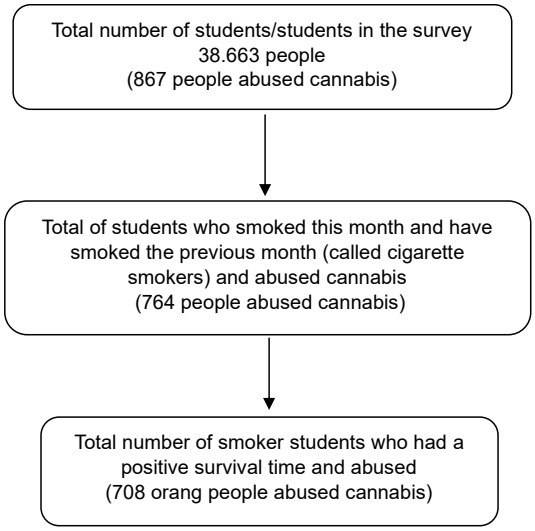

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46% (Agrawal et al., 2013). Then the Power of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 - 35 cigarettes/week, >35 - 70 cigarettes/week, >70 - 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 - 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet et al., 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 - 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4

Variable		Total N = 708	Percentage (%)
Smoking frequency	Rarely smoking	64	9.0
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Regarding the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years (Mayet et al., 2011)

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ*value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Prince van Leeuwen et al., 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhonen et al., 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 - 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 - 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 - 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens et al, 2007 in (Mayet et al., 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Weinberger et al., 2018; Hindocha et al., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen et al., 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet et al., 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *p*value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3

>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	P<0.0001 Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 - 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarely cigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking < 5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking > 7 – 35 cigarettes/week was 0.85, and the group with a frequency > 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life - based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal et al., 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal et al., 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

13. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 - 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 - 3,3).
14. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 - 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 - 5.3).

15. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 - 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		**B**	**SE**	**PValue**	**HR**	**95% CI**
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Prince van Leeuwen et al., 2011). Other previous studies also revealed that alcohol and cannabis could occur simultaneously (Brière et al., 2011; Subbaraman & Kerr, 2015). The second confounder in the correlation between the frequency of cigarette smoking and canabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Prince van Leeuwen et al., 2011). Meanwhile, various studies show that a history of

parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen et al., 2008; Scherrer et al., 2012).

The third Confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research showed that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen et al., 2008; Scherrer et al., 2012).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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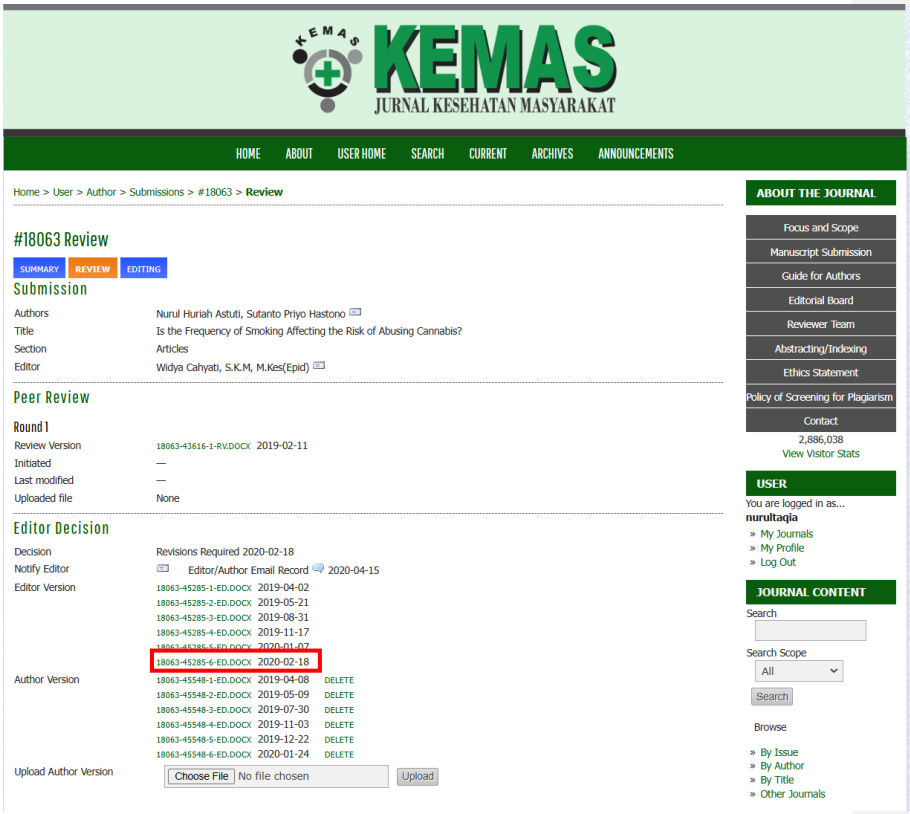
12. Menerima tanggapan final dari jurnal KEMAS (18 Februari 2020)



Is the Frequency of Cigarette Smoking Affecting the Risk of Abusing Cannabis?

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ABSTRACT

The results of previous study found that teens that had a cigarette smoking habit were 14 times more likely to smoke cannabis than those who did not smoke. This study aims to determine the relationship between the frequency of cigarette smoking and cannabis abuse done through survival analysis. The research samples were 708 students of cannabis abusers who were previously preceded by smoking. The results of this study found that durability or length of time for abusing cannabis was mostly 1 – 4 years. The Wilcoxon test results concluded that there was a difference in survival to abusing cannabis among the frequency groups of smoking. Multivariate analysis also showed that the

more number of cigarettes consumed, the greater the risk for abusing cannabis after being controlled by confounders. Conclusion of this study, the frequency of smoking affects the survival rate and the amount of risk to abusing cannabis.

Keywords: teens smokers, cannabis abuse, survival analysis

Introduction

Survey data of the Basic Health Research (Riskesdas) was found that the proportion of people who smoke every day and occasionally in Indonesia in 2013 was 29.3% of the total population (Kementerian Kesehatan RI, 2018). This number declined slightly in 2018, which was 28.8% of the population. However, if the proportion was calculated based on the total population of Indonesia in 2013 which was equal to 250 million people, then there were around 73.25 million Indonesian people who cigatette smoke every day and every so often in 2013. That number actually increased to 76.32 million since the population of Indonesia also enlarged to 265 million. Meanwhile, a survey of students in 18 provinces in Indonesia showed that one out of three or four students had ever smoked (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017).

Smoking habits are known to be the main cause of lung disease, like chronic obstructive pulmonary disease (Diaz-Guzman & Mannino, 2014). Smoking is said to cause respiratory problems and acute changes in the lung organs, including changes in respiratory flow resistance and pulmonary irritation. In early adulthood, smoking can affect respiratory function. Proper nutritional intake is preventive therapy which is known to prevent inflammation, obstruction, and lung function deficits. But unfortunately, research showed there were differences in nutritional intake between active smokers and nonsmokers (Gates *et al*., 2014; Indraswari *et al*., 2018). Smoking habits not only cause negative effects on active smokers but also second hand smoke or those who smoke cigarette smoke released by smokers (Öberg *et al*., 2011). A study showed a positive relationship between the length of time of other people's smoke exposure per day with urine cotinine levels and also there was a significant relationship between other people's smoke exposure by coworkers with urine cotinine levels (Nurjanah *et al*., 2014).

Cigarette smoking habits, based on the results of previous studies, would increase the risk of drug abuse especially cannabis (Astuti, 2016; Badiani *et al*., 2015; Hindocha *et al*., 2015; Mayet *et al*., 2011). Based on the theory, it is known that there are three theories related to the relationship of smoking with cannabis abuse. First theory is "the Gateway Theory" (GT) which states that the development of consumption of addictive substances follows an advanced process of the habit of consuming prohibited substances, such as cigarettes and/or alcohol. After consuming cigarettes/alcohol, it is predicted that it will continue to illicit substance abuse with types of soft drugs,

such as cannabis, and then followed by consuming prohibited types of hard drugs, such as cocaine or heroin (Secades-Villa *et al*., 2015; Prince van Leeuwen *et al*., 2011). Second, the theory of the Common Liability to Addiction (CLA) which states that substance consumption both licit and illicit is influenced by genetics and individual vulnerability, such as individual vulnerability to deviations and dependency in family conditions. Unlike the GT theory, CLA theory states that (a) the "choice" of what substances is consumed is first influenced by the factors mentioned above, namely genetics and individual vulnerability; and (b) There is no order in the process of developing substance abuse (Korhonen *et al*., 2008; Prince van Leeuwen *et al*., 2011). Third, the theory of "Route of Administration Model" (ROM) which states that the techniques of addictive substances used (for example inhalation or smoked) will affect the type of addictive substances that will be consumed later. This theory provides an explanation for why are smokers at risk of abusing cannabis? Because both smoking and abusing cannabis has the same way in terms of how to consume, this is smoked or inhaled (Prince van Leeuwen *et al*., 2011).

Survey data in Indonesia showed that cannabis was the most often drug type misused by all students in Indonesia (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Cannabis was also the most widely used of drug and the last year used of drug by Indonesian students surveyed by the National Narcotics Agency (BNN) and the University of Indonesia Health Research Center (PPKUI) in 2016 (Badan Narkotika Nasional Republik Indonesia & Pusat Penelitian Kesehatan Universitas Indonesia, 2017). Another study using a sample of teenagers living in the French metropolitan city explained the relationship between cigarette smoking habits and cannabis abuse. The results showed that the majority of cannabis abusers were preceded by cigarette smoking, only 2% of adolescent cigarette smokers and cannabis abusers that formerly started by using cannabis (Mayet *et al*., 2011).

Related to the frequency of cigarette smoking, research conducted on residents of Australian twins and siblings aged 12 - 46 years showed that the cigarette smoking habits routine was associated with an early opportunity to abuse cannabis and their first time to misused it. Each Hazard Ratio/HR (the risk of a group to experience hazard or failure or event if they were exposed rather than not exposed) was 2.35 (95% CI 2.16 - 2.56) and 3.49 (95% CI. 3.18 - 3.83) (Agrawal *et al*., 2013).

In this study, researchers analyzed the data from the National Survey on the Development of Drug Abuse and Narcotics Illicit Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). There were also three purposes of this study. First, knowing the time of endurance or the length of time (in years) to survive from the first time cigarette smoking until the very first time abuse cannabis. Second, knowing the rate of survival to cannabis abuse based on the frequency of cigarette smoking. Third, knowing the relationship between the frequency of cigarette smoking to the survival of cannabis

abuse after being controlled by a variable history of drinking alcohol, families exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence.

Method

The study design used in this study followed the study design conducted on the data used, namely the National Survey on the Development of Illicit Drug Abuse and Circulation in Student Groups in Indonesia in 2011 conducted by the National Narcotics Agency (BNN) and the Health Research Center of Indonesia University (PPKUI). The cross sectional study design was also used in the survey.

The study populations in this research were middle school, high school and college students who became respondents in the National Survey on the Development of Illicit Drug Abuse and Circulation in student groups in 2011 which were around 38,663 people. The samples of this study were students who smoked in the last month/in this month and students who had smoked in previous months, and assumed smoking habits preceded or coincided with misused of cannabis Hence, after being selected only for smokers (smokers this month and smokers in the previous month) and it had a positive survival time (smoking habit preceded or coincided with cannabis abuse), then total sample prepared for the analysis was 708 people (Figure 1).

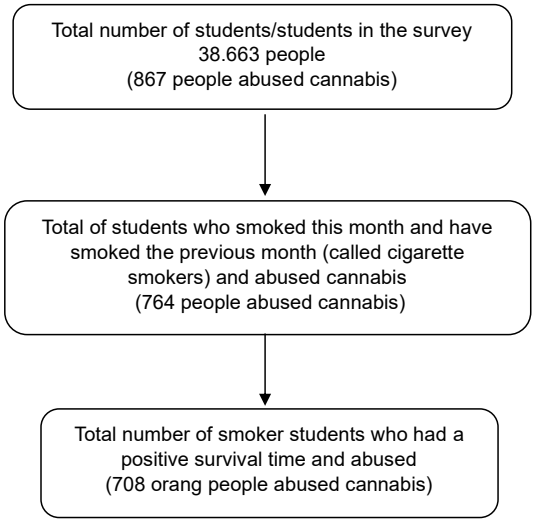

Figure 1. Research Sample Restriction

Based on the large sample formula according to Machin (1997) in (Agrawal *et al*., 2013) for survival analysis, then HR = 3.49 and $\pi 1$ (the proportion of cannabis abusers in routine cigarette smokers) was 55% and $\pi 2$ (the proportion of cannabis abusers on non-routine cigarette smokers) was 46%. Then the Power of the test in 708 samples analyzed was more than 99%.

Furthermore, to facilitate the interpretation of the analysis results, the researchers did the following related data. First, the value of survival time 0 to less than 0.5 (0 < survival time value <0.5) was recoded to 0.5 (there were 103 respondents with a value of 0 and 332 respondents with a value between 0.0082 to 0.4328). Second, the researchers made changes to the frequency group of smoking from secondary data used. Initially the frequency of smoking was divided into 7 groups, namely rarely smoking, <5 cigarettes/week, ≥5-7 cigarettes/week, >7 - 35 cigarettes/week, >35 - 70 cigarettes/week, >70 - 140 cigarettes/week, and >140 cigarettes/week, then the researcher recoded it into four groups, namely rarely smoking, <5-7 cigarettes/week, >7 - 35 cigarettes/week, and > 35 cigarettes/week. The cut-off determination of the four groups was based on the closeness of the line on the Kaplan Meier curve The rare definition of smoking referred in this study is those who did not cigarette smoking on the month when the interview was conducted.

Results and Discussion

The results of this study indicated that the majority of cigarette smokers who abused cannabis were male (93.4%); the age range of the youngest cigarette smoker was 7 years (2.8%) and the oldest was 21 years (0.1%); the majority started cigarette smoking at the age of 10-14 years (60%). The mean/average age of starting smoking was 13.15 years and the median was 13 years. The average age or middle age of the first time cigarette smoking obtained in this study was almost the same as the results of the study on a sample of teenagers living in French metropolitan city that showed the average age at first smoking was 13.4 years (Mayet *et al*., 2011).

Table 1. Frequency Distribution of Smoker Students that Misused cannabis in Indonesia in 2011

Variable		Total N = 708	Percentage (%)
Age of starting smoking	<10 years	55	8
	10 – 14 years	428	60
	15 – 19 years	219	31
	20 - 24	6	1
Age of using cannabis	5 – 9 years	2	0.3
	10 – 14 years	153	21.6
	15 – 19 years	464	65.6
	20 – 24 years	86	12.1
	25 – 29 years	3	0.4
Smoking frequency	Rarely smoking	64	9.0

Variable		Total N = 708	Percentage (%)
	<5–7 cigarettes/week	132	18.6
	>7–35 cigarettes/week	205	29.0
	>35 cigarettes/week	307	43.4
Length of time/survival time from smoking to misusing cannabis	1 – 4 years	435	61.5
	5 – 9 years	159	22.5
	10 – 14 years	11	1.5
	15 – 19 years	103	14.6

Regarding the early age of abusing cannabis, the youngest one was 8 years (0.3%) and the oldest one was 25 years (0.4%). However, the majority began to abuse cannabis at the age of 15-19 years (65.6%). The mean age of starting cigarette smoking was 16.19 and the median age of starting to abuse cannabis was 16 years. The average age of misusing cannabis in this study slightly differed from other studies which got an average age of misusing cannabis was 15.1 years or ranging from 15 years (Mayet *et al*., 2011)

The researchers then carried out a further analysis of the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis. Through correlation analysis and linear regression, the value of r = 0.551 and the value of *ρ* value <0.0001 was obtained. Thus, it could be concluded that the correlation between the first time age of cigarettes smoking and the first time age of abusing cannabis showed a strong and positive pattern of relationships. This cannabis. These conclusions corroborate predictions obtained from previous studies stating that the age at first cigarette smoking will increase the risk of misusing cannabis (Prince van Leeuwen *et al*., 2011). Other research also found that cigarette smoking before the age of 13 years is an important and strong predictor of abusing cannabis (Korhonen *et al*., 2008).

In addition, the results of Kaplan Meier's analysis found that the length of time for abusing cannabis in student cigarette smokers who misused cannabis was a minimum of 0.5 years (14.5%) and a maximum of 13 years (0.3%), while the most was 1 - 4 year (61.5%). Whereas the mean time interval was 3.10 years (95% CI: 2.9 - 3.3) and the median (50% sample) was 2.0 years (95% CI: 1.8 - 2.2).

Table 2. Mean and Median Time Intervals from the First Start of Smoking to Misusing Cannabis of Student Smokers that Abused Cannabis in Indonesia in 2011

Number of Sample (n)		Mean	Median
708	Value	3.1	2.0
	95% CI	2.9 – 3.3	1.8 – 2.2

The results of this study were in line with other studies which showed that cigarette smoking will open up opportunities for abusing cannabis in a relatively short time and have a strong relationship with cannabis drug abuse (Guxens *et al*, 2007 in Mayet *et al*., 2011). Moreover, cigarette smoking habits also has the potential to cause cannabis abuse, where cigarette smoking precedes cannabis abuse (Weinberger *et al*., 2018; Hindocha *et al*., 2015). The results of this study also reinforced the awareness of the behavior of cannabis abuse in cigarette smokers. That is, when people start cigarette smoking then it will not be up to five years, they will probably start consuming other types of addictive substances such as cannabis regardless of how fast the process starts from cigarette smoking to abusing cannabis. The outcomes of this study were also in line with the theory of Route of Administration which predicts that the type of addictive substance used today will affect other types of addictive substances consumed in the future. In more detail, it is explained that those who cigarette smoke will have the opportunity to abuse cannabis because the way to consume these two substances is similar, namely by inhalation (Van Leeuwen *et al*., 2011). Besides, the results of this study were indeed in accordance with "The Gateway Theory" (GT) which states that consuming cigarettes and cannabis is a sequential process. This means that consuming cigarettes or alcohol will potentially be followed by other substance abuse in the hard drug use group, such cannabis (Mayet *et al*., 2011).

Meanwhile, if it was analyzed based on the frequency group of smoking, the median length of time from first cigarette smoking to abusing cannabis indicated that those who rarely cigarette smoke till cigarette smoke with a frequency of 35 cigarettes/week have a 2-year abuse period, while students who smoke with a frequency of> 35 cigarettes/week have longer time to abuse Cannabis, i.e. 3 years (table 3). The Log Rank Test results showed a value of *ρ* value <0, 0001 which means that a difference in the length of survival time to abusing cannabis is based on the frequency of cigarette smoking. Though, it is not known exactly why those who smoke more than 35 cigarettes a day have a longer survival time to abuse cannabis.

Table 3. Mean and Median Length of Time from First Time Smoking to Misusing Cannabis Based on the Smoking Frequency of Student Smokers that Abused Cannabis in Indonesia in 2011

Cigarette Smoking Frequency	Mean		Median	
	Value (years)	95%CI	Value (years)	95%CI
Rarely smoking	3.5	2,732 – 4,331	2	1.4 – 2.5
<5 – 7 cigarettes/week	2.6	2,243 – 3,045	2	1.6 – 2.4
>7 – 35 cigarettes/week	3.7	2,427 – 3,017	2	1.7 – 2.3
>35 cigarettes/week	3.5	3,206 – 3,729	3	2.7 – 3.3
Relatively	3.1	3,926 – 3,282	2	1.8 – 2.2
Log Rank Test (Mantel-Cox)	p<0.0001; Chi-Square : 18,176 ; df = 3			

The results of life table analysis showed that at intervals of 0 - 4 years, the survival rate of cigarette smoking groups seen as a cumulative probability of survival (End) was 0.98. This meant that at intervals of 0-4 years, as many as 98% of students who rarely cigarette smoke still have not misused cannabis or at intervals of 0 – 4 years there were 2% of students who rarely cigarette smoke though abuse cannabis. The survival rate to abusing cannabis at these intervals was increasing based on the increasing number of cigarettes consumed. Students with a frequency of smoking < 5 – 7 cigarettes/week was 0.94, the group with the frequency of smoking > 7 – 35 cigarettes/week was 0.85, and the group with a frequency > 35 cigarettes/week was 0.80. Likewise, the next time interval has the same pattern, namely the more the number of cigarettes consumed, the more survival rate for abusing cannabis increased (Table 4).

Unfortunately, the researchers did not get the results of other studies that revealed the value of the survival rate of cannabis abuse based on the frequency of cigarette smoking so that researchers could not compare the results of this study with other studies. However, according to the researchers, the results of this study corroborate previous research which stated that those who cigarette smoke regularly (100 or more cigarettes in life - based on the standards of the Centers for Disease Control USA, 2007) are at higher risk for getting an opportunity to abuse cannabis and more early to abuse cannabis (Agrawal *et al*., 2013). This condition is increasingly driven by the discovery that those who routinely smoke feel the pleasure faster when they first abuse cannabis than those who do not routinely cigarette smoke (those who have never cigarette smoked or have ever cigarette smoked but never more than 100 cigarettes in their lifetime) (Agrawal *et al*., 2013).

Table 4. Life Table of Cannabis Abuse Based on Smoking Frequency of Student Smokers in 2011

Smoking Frequency	Time Interval	Number of "Safe" Subjects at the beginning of the interval	Number of Sensors during Interval	Number of Events During Interval	Cumulative Probability at the End
Rarely smoking	0	4,085	3,108	43	0.98
	5	934	807	17	0.95
	10	110	98	4	0.89
	15	8	5	0	0.89
	20	3	2	0	0.89
	25	1	1	0	0.89
< 5 – 7 cigarettes/week	0	3,149	2,552	107	0.94
	5	490	419	24	0.86
	10	47	39	1	0.83
	15	7	5	0	0.83
	20	2	2	0	0.83
>7 – 35 cigarettes/week	0	1,746	1,199	171	0.85
	5	376	291	33	0.73
	10	52	45	1	0.70
	15	6	3	0	0.70
	20	3	3	0	0.70
>35 cigarettes/week	0	1,399	640	217	0.80
	5	542	383	85	0.61
	10	74	54	5	0.54
	15	15	12	0	0.54
	20	3	1	0	0.54
	25	2	2	0	0.54

The final model of multivariate analysis showed that the history of drinking alcohol, families exposed to alcohol and/or drugs, separated from parents at least six months, and peer influence were confounding variables on the relationship between the frequency of cigarette smoking and cannabis abuse in 2011 in Indonesia (Table 5).

This final model also showed the pattern that the higher the frequency of cigarette smoking or the more number of cigarettes consumed by student smokers in Indonesia in 2011, the faster the hazard/risk value for abusing cannabis compared to student smokers in Indonesia who rarely cigarette smoking in 2011 (table 5). Overall, the final model explains:

16. Hazard ratio/risk for the occurrence of cannabis abuse of student smokers in Indonesia in 2011 who smoke with a frequency <5 - 7 cigarettes/week was 2.5 times faster than students in Indonesia who rarely smoke in 2011 after being controlled by variable of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 1,8 - 3,3).
17. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarette smokers who smoke with a frequency >7 - 35 cigarettes/week was 4.0 times faster than students in Indonesia in 2011

who rarely cigarette smoke after being controlled by a history of drinking alcohol, family exposed to alcohol and/or drugs, separate from parents at least for six months, and peer influence (95% CI: 3.0 - 5.3).

18. Hazard ratio/risk for the occurrence of cannabis abuse in student cigarettes smokers who smoke with a frequency of >35 cigarettes/week was 4.6 times faster than students in Indonesia in 2011 who rarely cigarette smoke after being controlled by a variable drinking alcohol history, family exposed to alcohol and or drugs, separate from parents at least for six months, and peer influence 95% CI: 3.5 - 6.0).

Table 5. Final Model of the Correlation between the Frequency of Smoking and Status of Cannabis Abuse of Student Smokers in Indonesia in 2011

Variable		B	SE	P Value	HR	95% CI
Cigarette Smoking Frequency	< 5 – 7 cigarettes/week (1)	0.910	0.154	<0.0001	**2.5**	**1.8 – 3.3**
	>7 – 35 cigarettes/week (2)	1.378	0.147	<0.0001	**4.0**	**3.0 – 5.3**
	>35 cigarettes/week (3)	1.521	0.143	<0.0001	**4.6**	**3.5 – 6.0**
History of Drinking Alcohol		1.341	0.117	<0.0001	3.8	3.0 – 4.8
Alcohol and/or Narcotics Exposed Families	Intermediate Exposure	-0.230	0.088	0.009	0.8	0.7 – 1.0
	Bad Exposure	0.326	0.343	0.343	1.4	0.7 – 2.7
Separate from parents at least for six months		0.234	0.124	0.059	1.3	1.0 – 1.6
Peer influence	Good Influence (1)	1.675	0.094	<0.0001	5.3	4.4 – 6.4
	Bad Influence (2)	1.882	0.124	<0.0001	6.6	5.1 – 8.4
Separate from parents at least for six months*T-Cov		-0.081	0.031	0.010	0.9	0.9 – 1.0

The first confounder found in this study was a history of drinking alcohol. The history of drinking alcohol was indeed found in several studies as a risk factor for abusing cannabis. Research conducted in Dutch adolescents, for example, showed that teens who drank alcohol at an early age would increase their risk of abusing cannabis with a hazard ratio of 1.43 and 95% CI: 1.2 1.7 (Prince van Leeuwen *et al*., 2011). Other previous studies also revealed that alcohol and cannabis could occur simultaneously (Brière *et al*., 2011; Subbaraman & Kerr, 2015). The second confounder in the correlation between the frequency of cigarette smoking and canabis abuse was a family exposed to alcohol and drugs. This is in accordance with the Common Liability (CL) theory which states that the use of prohibited or non-prohibited substances is influenced by genetics and individual vulnerability. Including individual vulnerability is the vulnerability of a person to commit deviant behavior and family history of substance dependence (Prince van Leeuwen *et al*., 2011). Meanwhile, various studies show that a history of parents who experience substance abuse (including drugs and alcohol) is an important risk factor for experiencing drug abuse for someone (Korhornen *et al*., 2008; Scherrer *et al*., 2012).

The third confounder was ever separated from parents for at least six months. Conceptually, students who live separately from their parents will increase their risk of committing deviant behavior due to weak supervision and communication with parents. This weak parental supervision is an important factor in drug abuse and other deviant behavior. The study found that children who do not live with their parents, their mothers or fathers will increase their risk of experiencing emotional distress, doing deviant behavior, and drug abuse, including cannabis although the impact of these conditions does not always occur (Hemovich & Crano, 2009). The last confounder was peer influence. Having peers who use drugs and/or alcohol will surely increase the chances of being offered drugs and/or alcohol. Research showed that friends who experience substance abuse (drugs, smoking, and drinking alcohol) are also risk factors for adolescents to experience drug abuse (Korhornen *et al*., 2008; Scherrer *et al*., 2012).

The results of this multivariate analysis revealed that the correlation between the frequency of cigarette smoking and cannabis abuse of student cigarette smokers in Indonesia in 2011 might actually be influenced by other conditions owned by cigarette smokers such as history of drinking alcohol, families exposed to alcohol and or drugs, have lived separately from parents for a minimum of six months, and have peer influence. However, through multivariate analysis that has been done, the four factors have been controlled. This means in the correlation between the frequency of smoking and cannabis abuse, the four confounding variables have been identified by analyzing the differences in the distribution of risk factors/confounding between the group of cannabis abusers and non-cannabis abusers.

Conclusion

This study concluded that the more cigarettes consumed the more survival rate of abusing cannabis increased. The more cigarettes consumed, the higher the hazard/risk of abusing cannabis compared to cigarette smokers who rarely smoked.

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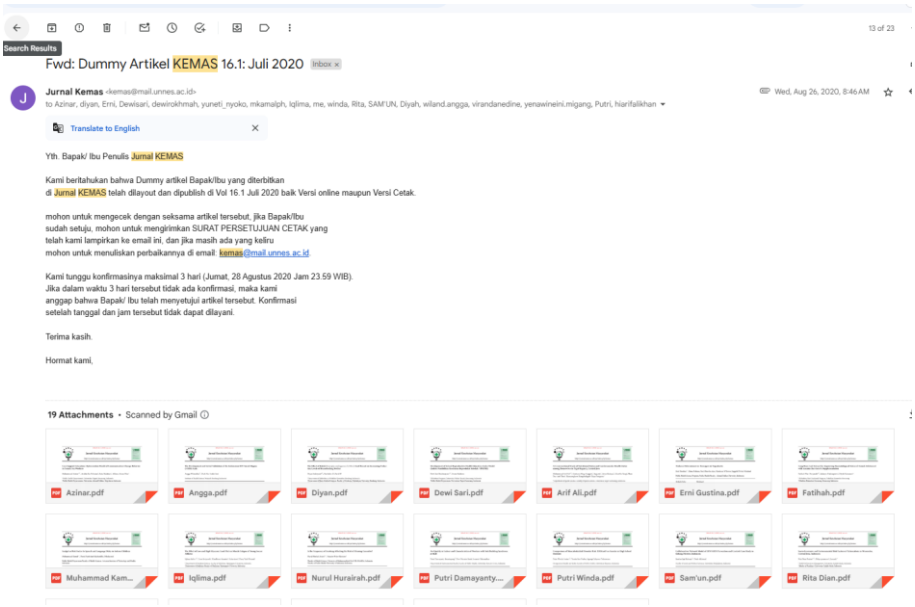

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