# GLOBAL MEDICAL & HEALTH COMMUNICATION



# Global Medical & Health Communication

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The submitted manuscript must be the article that has never been published, and the author must ensure that all co-authors have agreed by signing a statement on the seal. Download template of the ethical statement (free plagiarism) here. The manuscript is an original article free from plagiarism. When the article published in another journal then in the next journal, the article will be disallowed.

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Table title is the typed center, font size 10 pt, bold, initial letter of each word written with capital letter, except conjunctions. The titles are numbered and written on top of the table. Example: Table 3 *Neisseria gonorrhoeae* Resistance to 8 Types of Antimicrobials in 20 Specimens. Table, no vertical dividing line, and there are only three horizontal borderlines. Created tables in sequence two spaces from the text. Table descriptions and abbreviations are placed in the table description, not on the table title.

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#### Introduction

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#### Conclusion(s)

The conclusion is submitted by the results obtained by the researcher and written briefly and clearly in two or three sentences.

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#### Acknowledgement

Acknowledgments should be provided to research contributors without writing a degree.

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Zhang B, Kunde D, Tristram S. Haemophilus haemolyticus is infrequently misidentified as Haemophilus influenzae in diagnostic specimens in Australia. Diagn Microbiol Infect Dis. 2014;80(4):272– 3.

#### Books and Other Monographs Editor as Author

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#### **RESEARCH ARTICLE**

#### Effect of Physical Activity and Vitamin D Status on Geriatrics Obesity

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#### Abstract

Vitamin D levels in the body are decreased in tropical countries. This may be due to a decrease in physical activity, age and obesity to be a risk factor for decreased vitamin D levels. This study aims to determine differences in the level of physical activity in geriatrics obesity and non-obesity to vitamin D. This research method is observational with case-control study design. The study was conducted at Public Health Center Taman, Sidoarjo district, East Java in March–July 2017. Geriatric were grouped into 2 groups of obese and non-obese by using body mass index (BMI) calculations. Respondents were given a questionnaire to assess the level of physical activity and vitamin D status. Furthermore, an assessment of physical activity and vitamin D status were performed on each respondent. The first questionnaire was given to 30 people for the validity test (r>0.361) and reliability test (Cronbach alpha=0.731). The results showed no significant differences in physical activity levels between the two groups (chi-square, p=0.883). The assessment of vitamin D status can be seen as a significant difference (chi-square, p=0.042). In conclusion, geriatrics with obesity and non-obesity had similar levels of physical activity, but vitamin D status in obesity tended to be lower than non-obese.

Key words: Geriatrics, obesity, physical activity, vitamin D

#### Pengaruh Aktivitas Fisik dan Status Vitamin D terhadap Obesitas Geriatri

#### Abstrak

Kadar vitamin D dalam tubuh semakin menurun di negara yang beriklim tropis. Hal ini dapat disebabkan oleh penurunan aktivitas fisik, usia, dan obesitas menjadi faktor risiko penurunan kadar vitamin D. Penelitian ini bertujuan mengetahui perbedaan tingkat aktivitas fisik pada geriatri obesitas dan nonobesitas terhadap status vitamin D. Metode penelitian ini adalah observational dengan desain penelitian kasus kontrol. Penelitian dilakukan di Puskesmas Taman, Kabupaten Sidoarjo, Jawa Timur pada bulan Maret–Juli 2017. Responden geriatri dilakukan penimbangan berat badan dan pengukuran tinggi badan untuk dikelompokkan menjadi 2 kelompok, yaitu kelompok obesitas dan nonobesitas dengan menggunakan perhitungan indeks massa tubuh (IMT). Responden diberikan kuesioner untuk menilai tingkat aktivitas fisik dan status vitamin D. Selanjutnya, dilakukan penilaian aktivitas fisik dan status vitamin D pada tiap-tiap responden. Kuesioner telah diberikan kepada 30 orang untuk dilakukan uji validitas (r>0,361) dan uji reliabilitas (Cronbach alfa=0,731). Hasil penelitian memperlihatkan tidak terdapat perbedaan tingkat aktivitas fisik yang signifikan antara kedua kelompok (chi-kuadrat, p=0,883). Pada penilaian status vitamin D dapat terlihat perbedaan yang signifikan (chi-kuadrat, p=0,042). Simpulan, geriatri dengan obesitas dan nonobesitas memiliki tingkat aktivitas fisik yang sama, sedangkan kadar vitamin D pada obesitas cenderung lebih rendah dibanding dengan nonobesitas.

Kata kunci: Aktivitas fisik, geriatri, obesitas, vitamin D

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#### Introduction

The decrease of vitamin D levels in society is increasing and is almost spread worldwide regardless of age, gender, origin, location, and food. The increasing rate of declining vitamin D levels not only occurs in developing countries but also in developed countries. Several developed countries in America, Europe, Australia, Africa, the Middle East, and South Asia are also affected. The highest number of vitamin D deficiency is mostly found in China, South America, India and the Middle East with a prevalence that varies from 30% to 100%.<sup>1</sup> The decreasing of vitamin D levels to below 20  $\mu$ g/mL reaches 90.5% in the Malay ethnics while in the Chinese ethnics, it only reaches 55%.<sup>2</sup>

Various kinds of risks can be caused by vitamin D deficiency because the body's system does not work optimally, so that it will trigger various diseases. Vitamin D can also be categorized as an antioxidant, so free radicals that enter the body can be neutralized.<sup>3</sup> Free radicals and antioxidant imbalances in the body can also increase the incidence of disease.<sup>4</sup> Many diseases can result from vitamin D deficiency such as cardiovascular disease, diabetes, chronic kidney failure, and asthma.<sup>5–7</sup>

The cause of the decrease in vitamin D levels in the body is less sun exposure caused by various factors, namely obesity, age, and decreased physical activity.<sup>8-10</sup> Weight gain may be associated with a decrease in vitamin D levels. It is probably because of the relation of vitamin D gene receptor (VDR) polymorphism which gives a difference in VDR expression so that it can inhibit adiposity differentiation and increase adipose mass. In addition, increased adiposity may lead to increasing levels of parathyroid hormone and changes calcium to adipocytes, which increases lipogenesis.<sup>11</sup> Another triggering factor is a decrease in the leptin hormone in obese patients because vitamin D is an important factor in producing leptin. Inhibition of leptin synthesis will result in increased appetite and obesity.8

Age factors can trigger a decrease in vitamin D levels. Physically, geriatrics are less mobile and have poor nutritional status. In addition, there are physiological processes that aggravate the decline in vitamin D levels in the body such as a decrease in vitamin D production in the skin after the exposure to sunlight caused by skin atrophy, eating foods that are low in vitamin D, gastrointestinal absorption disorders, and a decrease in production 1,25(OH)2D in kidney.<sup>9</sup>

Physical activity is also associated with a decrease in vitamin D levels. This is because the previous risk factors, namely age, and obsession, can directly affect the level of physical activity. Increased physical activity is related to the 25OHD increase caused by muscle movements during exercise. Physical activities carried out in the daily activities allow sufficient amounts of sunlight exposure to produce vitamin D.<sup>12</sup> This study aims to compare vitamin D status and physical activity using questionnaire so that it can predict the risk of vitamin D deficiency in obese geriatrics.

#### Methods

This research was an observational study with a case-control design. The study was conducted in the geriatric age group at Public Health Center Taman, Sidoarjo, East Java (No.: 070/5099/209.4/2017). The selection process was carried out according to the inclusion criteria in the elderly age group such as disability, kidney failure, consumption of anti-seizure drugs and visual impairments, while the exclusion criteria if the respondent resigns as a study sample.<sup>13</sup>

Geriatric respondents who have been interviewed will be divided into 2 groups: 52 obese people and 60 non-obese people by weighing and height measurement, to be assessed by calculating the body mass index (BMI). Sampling used was non-random sampling with purposive sampling technique with a significance level of 5% and a test strength of 95%. Then the two groups were given a question regarding physical activity and vitamin D status.

The physical activity questionnaire that will be used in this study is the International Physical Activity Questionnaire (IPAQ)<sup>14</sup> and vitamin D status.<sup>15–17</sup> The questionnaire has been tested for validity and reliability test on 30 homogeneous respondents with research respondents. Validity test is done based on the calculated r value (Corrected Item–Total Correlation)>r table. The r table is obtained from the product moment table with a significant level of 5%, if the r value>0.361 so the question is declared valid. While the reliability test uses the Cronbach alpha correlation. Cronbach alpha value is said to be reliable if the questionnaire reliability test value is equal to or more than 0.6. Physical activity categories divided into 3 groups, namely light physical activities (cleaning the house, shopping, doing yoga), moderate physical activities or physical activities which can only increase heart work (dancing, gardening, doing light exercise), and heavy physical activities or physical activities that can make breathing faster and increase the work of the heart (running, fast cycling, climbing, doing competitive sport).<sup>12</sup>

Data on physical activity and vitamin D status analyzed by using the chi-square test to see differences in physical activity and vitamin D status in the obese and non-obese geriatric groups.

#### Results

Characteristics of respondents in both groups were present in Table 1. It was seeing more women respondents than men in groups. 112 respondents were found 19 men (17%) and 93 women (83%), while 47 people aged 45–59 years (42%), 50 people aged 60–66 years (45%), and 15 people aged >70 years (13%).

The results of the value distribution of questionnaires about physical activity in both groups are present in Table 2. Level low of physical activity in the obesity group was 47 respondents (90%) and the non-obese group also shows a low level of physical activity that was equal to 54 respondents (92%).

The distribution results of the vitamin D status category are present in Table 3. Vitamin D status in the obese and non-obese groups was mostly in the deficiency category. The obesity group was 42 respondents (81%), while in the non-obese group there were 38 respondents (63%).

The results of data analysis by chi-square test in both groups on the level of physical activity are in Table 4 and vitamin D status in Table 5. Based on the results of data analysis with chi-square test showed the p value at the level of physical activity (Table 4) was 0.883 (p>0.05), while the value of vitamin D status (Table 5) showed p value=0.042 (p<0.05).

#### Discussion

Geriatrics is a natural aging process that is sure to happen to everyone. The aging process is accompanied by a decrease in physical activity, organ function and immune system and changes in diet. This results in geriatric susceptibility to disease.

Vitamin D is often called prohormones, which have 2 active forms of vitamin D2 (ergocalciferol)

Groups **Characteristics Obesity (n=52)** Non-obesity (n=60) Percentage Frequency Frequency Percentage Gender Man 8 15 11 18 Woman 44 85 49 82 Age (year) 45-59 21 40 26 43 60-69 25 48 25 42 >70 6 12 9 15

Table 1 Distribution of Respondents Based on Gender and Age

#### Table 2 Distribution of Levels of Physical Activity in Both Groups

	Groups							
<b>Physical Activity</b>	Obesity	y (n=52)	Non-obes	ity (n=60)				
	Frequency	Percentage	Frequency	Percentage				
Low	47	90	54	92				
Medium	4	8	4	5				
High	1	2	2	3				
Total	52	100	60	100				

	Groups							
Vitamin D Status	Obesity	/ (n=52)	Non-obesity (n=60)					
	Frequency	Frequency Percentage		Percentage				
Deficiency Non-deficiency	42 10	81 19	38 22	63 37				
Total	52	100	60	100				

#### Table 3 Distribution of Vitamin D Status

Table 4 Chi-square Test Results of Physical Activity Level

Chonne	I	Physical Activit	– Total	Chi aguana Tast		
Groups	Low	Medium	High		Chi-square Test	
Obesity	47 (90%)	4 (8%)	1 (2%)	52 (100%)	p value=0.883	
Non-obesity	54 (92%)	4 (5%)	2 (3%)	60 (100%)	(p>0.05)	
Total	101	8	3	112		
······································						

p<0.05=significant

Table 5 Chi-square Test Results of of Vitamin D Status

Crowna	Vitami	in D Status	Total	Chi aguara Tagt	
Groups	Deficiency	Non-deficiency	Total	Chi-square Test	
Obesity	42 (81%)	10 (19%)	52 (100%)	p value=0.042	
Non-obesity	38 (63%)	22 (37%)	60 (100%)	(p<0.05)	
Total	80	32	112		
1 10 1					

p<0.05=significant

and vitamin D3 (cholecalciferol). Ergocalciferol comes from vegetable sources, while cholecalciferol is derived from animal sources, which is formed by ultraviolet B radiation at 7-dehydrocholesterol. Furthermore, vitamin D is converted into an active hormone so it can be used in mineral metabolism and physiological functions of the body. Vitamin D2 and vitamin D3 have the same potential.<sup>7</sup>

Vitamin D in humans serves to maintain serum calcium concentration and increase phosphorus absorption, but does not regulate phosphorus concentration in the blood but depends on renal excretion. Vitamin D in the form of 1,25(OH)2D also works with parathyroid and calcitonin hormones to maintain calcium concentration in plasma within the normal range. This is done by adjusting the efficiency of the small intestine to absorb calcium from the diet, mobilizing calcium from the bones and tubular reabsorption of calcium in the kidneys. Parathyroid hormones and 1,25(OH)2D together stimulate osteoblasts to induce pre-osteoclast maturation into osteoclasts, thereby increasing bone resorption.<sup>7,18</sup>

The physical activity is a body movement that results in greater energy expenditure than at rest. The physical activity carried out in the outside environment, with sun exposure, will provide an increase in vitamin D in the body.<sup>19</sup>

Vitamin D is one of the important vitamins in geriatrics because it has the ability to increase endurance. The main source of vitamin D is easy to obtain, which is through exposure to sunlight. However, several factors can inhibit the formation of vitamin D such as less physical activity and obesity.<sup>20,21</sup>

The results show no difference between the level of physical activity in geriatric obesity and non-obesity. However, there were similarities between the two groups, most of which have a low level of activity. Whereas in vitamin D status, there was a significant difference between the geriatric obesity group and the non-obesity, although most of the vitamin D status in both groups is in deficiency status.

#### Conclusion

Geriatrics with obesity and non-obesity had similar levels of physical activity, but vitamin D status in obesity tended to be lower than nonobese.

#### **Conflict of Interest**

The authors declare no conflict of interest.

#### Acknowledgements

The researchers would like to thank the Public Health Center Taman, Sidoarjo, East Java in the data collection process.

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#### **RESEARCH ARTICLE**

#### The Effect of Mixed-Fruit Juice on Uterine Contractions and Cervical Dilatation During the First Stage of Delivery

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#### Abstract

Energy imbalance in delivery can inhibit the action of glycolytic enzymes and interfere with chemical reactions in muscle cells. These nuisances may interfere with uterine contractions that obstruct cervical dilatation. Therefore, mothers require a nutritional alternative which is practical, generates energy quickly and supplies glucose needed for uterine contractions. These can be fulfilled with a mixed-fruit juice beverage. Mixed-fruit juice consists of fruits, Tunisian dates, honey, and red beans. This study aims to analyze the effect of the mixed-fruit extract on uterine contraction and cervical dilatation during the first stage of delivery. This study used a randomized controlled trial design. The target population was all the mothers who would give birth in Bandung city in March-April 2017. The samples of this study were the gravida <4 who would give birth at the Pelayanan Obstetri Neonatal Emergensi Dasar/PONED (Basic Emergency Obstetric and Neonatal Care/BEONC) Puskesmas (Public Health Center) Ibrahim Ajie, Puter, Garuda, Pagarsih, and Padasuka, consisting of 30 subjects as the treatment group and other 30 subjects as the control group. Uterine contractions and cervical dilatation were measured clinically and recorded on partograph. The analysis of data was done using the chi-square test, independent t test, and Mann-Whitney test. The results showed that there was the effect of mix-juice on the frequency, the duration and the intensity of uterine contractions and cervical dilatation with p value<0.05 and relative risk (RR) values respectively of 1.3, 3.3, 2.6, 1.7. In conclusion, consuming mixed-fruit juice during the first stage of delivery give an impact on the progress of uterine contractions and cervical dilatation.

Key words: Cervical dilatation, mixed-fruit juice, uterine contractions

## Pengaruh Pemberian Minuman *Mix Juice* terhadap Kontraksi Uterus dan Pembukaan Serviks Selama Kala I Persalinan

#### Abstrak

Ketidakseimbangan energi saat persalinan dapat menghambat kerja enzim glikolitik dan mengganggu reaksi kimia dalam sel otot sehingga dapat menghambat kontraksi otot dan pembukaan serviks. Perlu alternatif nutrisi ibu bersalin yang praktis, cepat menghasilkan energi, dan memberikan asupan glukosa yang dibutuhkan untuk kontraksi uterus dalam bentuk minuman *mix juice. Mix juice* ini mengandung buah-buahan, kurma tunisia, madu, dan kacang merah. Penelitian ini bertujuan menganalisis pengaruh pemberian minuman *mix juice* terhadap kontraksi uterus dan pembukaan serviks selama kala I persalinan. Penelitian ini menggunakan desain *randomized controlled trial*. Populasi target adalah semua ibu yang akan melahirkan di Kota Bandung pada bulan Maret–April 2017. Sampel dalam penelitian ini adalah gravida <4 yang akan melahirkan di Puskesmas Pelayanan Obstetri Neonatus Emergensi Dasar (PONED) Ibrahim Ajie, Puter, Garuda, Pagarsih, dan Padasuka, yaitu 30 subjek pada kelompok perlakuan dan 30 subjek pada kelompok kontrol. Kontraksi uterus dan pembukaan serviks diukur secara klinis dan dicatat pada partograf. Analisis data menggunakan uji chi-kuadrat, uji t independen, dan Uji Mann-Whitney. Hasil penelitian didapatkan pengaruh pemberian minuman *mix juice* terhadap frekuensi, lama dan intensitas kontraksi uterus, serta pembukaan serviks dengan nilai p<0,05 dan nilai RR masing-masing sebesar 1,3; 3,3; 2,6; 1,7. Simpulan, pemberian minuman *mix juice* selama kala I persalinan berpengaruh terhadap kemajuan kontraksi uterus dan pembukaan serviks.

Kata kunci: Kontraksi uterus, minuman mix juice, pembukaan serviks

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#### Introduction

Delivering baby is the process of significant energy consumption which is regulated by the complex nervous system and hormonal response.1 Hormonal and metabolic changes along with physical and psychological adjustments during delivery can cause energy imbalance (glucose homeostatic disorder) and mental stress that can cause fatigue in delivery processes. The process of giving birth influenced by the power factor (power or uterus contractions), the birth canal (passage or cervix dilatation), and fetal factors (passenger or the move down of head). Inadequate uterine contractions and cervical dilatation can be affected by physical and psychological factors, including lack of energy supply, dehydration, ketoacidosis, and physical and mental fatigue.2-4

Inadequate uterus contractions and cervical dilatation can elevate the occurrence of prolonged delivery that can increase maternal and neonatal mortality and morbidity. According to the 2012 Indonesia Demographic and Health Survey (IDHS), the rates of prolonged labor were 35%.<sup>5</sup> Research conducted by the National Institutes of Health in San Francisco in 2014 showed that 13.9% of nulliparae had a prolonged second stage and 31% of them experienced over 2 hours of stage.<sup>6</sup>

Glucose is the primary metabolic substrate used by the uterus.<sup>2</sup> Lack of energy supply in the form of glucose will cause fatigue of the uterine muscles.3 If fatigue occurs, lactic acid accumulates that makes the glycolytic enzymes work is inhibited, interferes chemical reactions in muscle cells, and hampers the release of Ca<sup>2+</sup> ions, causing muscle contraction to be weakened or disrupted. A study conducted by Ebrahimzadeh et al.<sup>3</sup> confirms that fatigue causes changes in the pattern of uterine contractions and affects the progress of the delivery. Several factors influence this including metabolite production, changes in energy level and energy-producing enzymes, psychological conditions, and environmental factors.1,4

The production of metabolites and changes in the energy level of the mother during delivery fulfilled with adequate nutrition. Unfortunately, based on the results of a preliminary study on 30 mothers during delivery it was found that 87% of mothers still wanted to consume food at the first latent stage and after entering the active phase, it dropped to 40% due to the more frequent pain. In the second stage of delivery, only 6% of mothers consumed food and only in liquid form. The average number of calories that a mother consumed was only 30 kcal/hour. Although the mother can cope with her childbirth without food, this may bring detrimental effect on the delivery process to both mother and baby, such as prolonged delivery and delivery with actions.<sup>7,8</sup>

Insufficient maternal energy needs during delivery will cause fatigue.<sup>3</sup> Malin et al.<sup>8</sup> and Rahmani et al.9 recommend energy requirements during delivery, namely 50-100 kcal/hour to prevent fatigue. Nutritional intakes prioritized for fulfilling the energy needed for uterine contraction. The types of nutrients required are kinds of food that provide energy, hydrate and prepare for the postpartum period.<sup>10</sup> Ideal nutrition for maternity must have a similar quality, high carbohydrates, high calories, and low residue, as well as in the forms of liquid or semi-solid. The reason is that in the current stage of delivery there is an inhibition of gastric emptying. Thus, if given solid food the nutrients cannot be adequately absorbed.<sup>2,7</sup>

During maternity, mothers do not only need one nutrient to increase nutritional value and to adjust for the calories needed, but a combination of various ingredients (mixed-fruit juice) to get all the benefits. In this study, mixed-fruit juice consists of Tunisian dates, honey, boiled, dried red beans and fruits such as mangoes, oranges, and red guava. These ingredients chose because they contain monosaccharides in the forms of fructose and glucose which can be quickly transported into the blood, promptly produce energy, and strengthen people who are sick or who are experiencing extreme fatigue.<sup>11,12</sup>

Glucose available in the blood is an energy substrate used at the beginning of delivery (3–6 cm dilatation) while glycogen in the muscle used during further stages (7–10 cm dilatation and during the birth process). The longer the delivery processes, the lower is the glucose stored.<sup>13</sup> High glucose load during delivery causes the mother to require additional nutritional alternative that has good taste, is practical, has sufficient calorie needs as well as produces energy quickly. Therefore, it is necessary to make a mixed-fruit juice which is expected to be able to give impact on the adequate uterine contractions and progress of cervical dilatation during the first stage of delivery.

#### Methods

The method used in this study was a randomized

controlled trial (RCT). This study was conducted by measuring uterine contractions and cervical dilatation during the first stage of labor from both the treatment and the control groups. The treatment group consumed a mixed-fruit juice, while the control group had the freedom to eat and drink anything. The amount of intake in the two groups evaluated per 2 hours and the number of calories consumed calculated during the delivery process. This study conducted at five Pelayanan Obstetri Neonatal Emergensi Dasar (PONED) or the Basic Emergency Obstetric and Neonatal Care (BEONC) puskesmas (public health center) in Bandung city. They were Public Health Center Ibrahim Ajie, Puter, Garuda, Pagarsih, and Padasuka. The target population in this study were all mothers who would give birth in Bandung city.

Meanwhile, the accessible population in this study were the pregnant women with gravida <4 who would give birth at the PONED public health centers in Bandung city. Then the samples were taken using block randomization, specifically through permutation block. The number of samples needed was 30 subjects for each of the treatment group and the control group taken from March–April 2017.

The inclusion criteria were mothers who would give birth at the age of 20-35 years with gravida <4 came when in the latent phase, had average body mass index (BMI) before pregnancy of 18.5-24.9 kg/m<sup>2</sup>, were in a-term, single, and healthy pregnancies. Besides, the exclusion criteria included complications during pregnancy, complications during labor, specific food allergies, history of gastritis, and having metabolic disorders. Further, the drop-out criteria were not consuming drinks as much as 100 kcal/ hour, labor with actions, his abnormalities, fetal distress, and the prolonged first stage of the delivery >12 hours in primigravida and >8 hours in multigravida.

The procedure for making mixed-fruit juice began with determining the compositions of the nutrient contents of each ingredient, then formulating and conducting experiment until the three formulas. An organoleptic test was carried out to these three formulas to find out the best one. Afterward, two flavors created, guava and mango—finally, both variants facing the quality test, the microbial and *Escherichia coli* test.

Monitoring of the amount of mixed-fruit juice spent in the treatment group as well as the food and beverages consumed by the mothers in the control group during the first stage of labor was carried out by the enumerator. The results of the monitoring recorded in the specific form. Uterine contractions were measured every 30 minutes with manual palpation. The number, strength, and duration of contractions for 10 minutes were counted and observed using a partograph. The length of uterine contractions was also found using a stopwatch. Further, cervical dilatation was measured every four hours and or based on the theory of progression of cervical dilatation using the vaginal toucher and was observed using the partograph. Lastly, the data analysis of this study was implemented using the chi-square test, independent t test, and the Mann-Whitney test. This study aims to analyze the effect of the mixedfruit extract on uterine contraction and cervical dilatation during the first stage of delivery.

This study conducted after obtaining the feasibility permit from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Padjadjaran Bandung with No. 262/UN6.C10/PN/2017. This study applied three basic principles of research ethics, namely respect to a person, beneficence and nonmaleficence, and justice.

#### Results

The quality test analysis of mixed-fruit juice beverages was carried out at the Food Technology Laboratory of Universitas Pasundan Bandung with the following results (Table 1). Mostly the quality of the products met the beverage quality standards for maternity and *Standar Nasional Indonesia*/SNI (Indonesian National Standards) 01-7148-2005. However, the contents of proteins are lower while the carbohydrates are higher than the rules.

Both research groups similar in terms of age, occupation, BMI, gravida, cervical dilatation at the arrival time and anxiety levels explained in detail in Table 2. The results of t test show that there were no significant differences (p>0.05) between the treatment and the control groups in terms of age, occupation, BMI, gravida, cervical dilatation at the arrival time and anxiety levels.

The two research groups were compared in terms of uterine contractions and increased cervical dilatation during the first active stage was in Table 3. Table 3 shows that there are significant differences (p<0.05) between the group with mixed-fruit juice beverages and the group without mixed-fruit juice beverages in terms of

Test Type	Guava Mix Juice Variant	Mango Mix Juice Variant	Quality Standards (per 100 mL)
Water (%)	76.60	77.20	-
Ash (g)	0.01	0.01	Max. 1.1
Fat (g)	1.80	1.80	Min. 0.6
Protein (g)	1.80	1.80	3.2-4.4
Carbohydrate (g)	20.90	20.80	Max. 4.4
Calorie/energy (kcal)	107.00	105.00	Min. 65

Table 1 The Results of Quality Test Analysis of Mix Juice Beverages

#### Table 2 Characteristics of the Research Subjects

	Grou	<b></b>	
Characteristics	Treatment (n=30)	Control (n=30)	p Value*
Age (year)			
20-24	11	9	0.149
25-29	11	6	
30-35	8	15	
x (SD)	26.3 (4.5)	28.3 (5.5)	
Range	20-35	20-35	
Occupation			
Employed	8	10	0.573
Unemployed	22	20	
Body mass index (kg/m²)			
x (SD)	21.2 (1.8)	21.6 (1.8)	0.407**
Median	21.2	21.6	
Range	18.5-24.9	18.6-24.9	
Gravida			
Primigravida	14	12	0.602
Multigravida	16	18	
Cervical dilatation at arrival (cm)			
2	11	9	0.584
3	19	21	
Levels of anxiety			
None	23	26	0.453
Low	6	4	
Medium	1	0	

\*Chi-square test, \*\*Fisher's exact test

frequency, duration of uterine contractions, the intensity of uterine contractions, and cervical dilatation during the first active stage of labor. Also, mothers who did not get mixed-fruit juice beverages had higher risks on low frequency, duration, the intensity of contractions and cervical dilatation during the first stage of labor than those who got mixed-fruit juice beverages.

#### Discussion

The water levels in this mixed-fruit juice beverages were 76.6% (red guava variant) and 77.2% (mango variant). This was because the beverage products are mostly contained water. The levels of ash in the mixed-fruit juice beverages also met the quality standard of beverages. The higher

		Gre				
Categories	Cont	trol	Treatment		 p Value*	RR (95% CI)
	n=30	%	n=30	%	_	(95/0 01)
Uterine contractions during the first active stage						
Frequency (times)						
x (SD)	4.2 (	0.4)	3.5 (	0.5)		
Median	4		3		0.011**	1.30
Range	4-	5	3-	4	0.011	(1.07–1.59)
<4	30	100	23	77		
≥4	0	0	7	23		
Duration (seconds)						
x (SD)	46.3 (	(8.8)	40.0	(5.4)		
Median	45		38		0.000	3.29
Range	31–66		34-55		0.000	(1.67-6.47)
≤40	23	77	7	23		
>40	7	23	23	77		
Intensity						
Weak	18	60	7	23	0.004	2.571
Strong	12	40	23	77		(1.26–5.24)
Increased cervical dilatation (cm/hour)						
x (SD)	1.9 (0.7)		1.4 (0.7)			
Median	1.9	9	1.	3	0.039	1.73
Range	0.7-	3.0	0.3-	3.3		(1.00–2.97)
<2	19	63	11	37		
≥2	11	37	19	63		

Table 3	The	Effect	of	Intervention	on	Uterine	Contractions	and	Increased	Cervical
	Dila	tation								

\*Chi-square test, \*\*Fisher's exact test

the ash level in a food product, the worse is the quality of food products for the ash level reflects the level of cleanliness and purity of a material.<sup>14</sup> At the same time, the fat contents in the mixed-fruit juice beverages are higher than the standard level while the protein levels of the mixed-fruit juice beverages were lower than that from the SNI 01-7148-2005. However, this did not become an obstacle during this study because the fat and the protein levels in this study were not taken into account.

The carbohydrate levels in the mixed-fruit juice were higher than the standard of drink for pregnant women, because mothers in the labor process needed more glucose contained in high carbohydrates as the main source of nutrition in metabolism in the myometrium during labor. The longer the labor, the lower is the stored glucose. Therefore, higher glucose intake is needed during labor.<sup>13</sup>

In this study, the research subjects from the treatment group and the control group had the same features including age, occupation, BMI, gravida, dilatation at the arrival time, and anxiety levels. The age and BMI of the respondents were almost similar; still in the reproductive age with a range of 20-35 years old and were in the healthy BMI category of 18.50-24.99 kg/m<sup>2</sup>. Meanwhile, most of the research subjects from both groups were unemployed. Regarding the gravida, there was no significant difference between the treatment group and the control group because the gravida group respondents limited to the inclusion criteria, namely the gravida <4. Likewise, the cervical dilatation at the arrival time had also limited to the inclusion criteria, which

was <4 cm. Last, the levels of anxiety between the two groups did not have a significant difference, that the levels of tension of the research subjects were homogeneous.

One of the factors that can affect the progress of labor is power (uterine contractions). The more adequate contractions of the smooth muscle of the uterus will result in the thinning and widening of the cervix progressively.<sup>8</sup> One factor that can affect appropriate uterine contractions is nutrient intake. The results are following Abdel Ghani's<sup>15</sup> research in 2012, showing that oral consumption of nutrients in the form of zam-zam water proved to have a significant effect on the frequency and duration of uterine contractions. The study showed the blood glucose levels maintained between groups. If the blood glucose level is low, it can result in the formation of ketones which can interfere uterine contractility.

During the deliverv process highcarbohydrates, low-fat, and low-residue nutrients in the forms of liquid or semi-solid need to be easily absorbed. It also need to produce energy quickly that affect the structure and strength of uterine muscle contractions.<sup>2,7</sup> The ingredients contained in the mixed-fruit juice beverages were safe to be consumed, and they contained carbohydrates (glucose) as an energy source in the myometrium. Carbohydrates are the primary energy source that can be digested by the human body and glucose contained in carbs is the primary energy source in the body because some organs in the body only use glucose. Carbohydrates contained in these mixed-fruit juice beverages were monosaccharide type. Monosaccharides absorbed by the intestine and cannot be hydrolyzed further into simple sugars.16

Once entered through the mouth, the carbohydrates in the mixed-fruit juice will go through a chemical digestion process, namely the digestive process aided by enzymes. The tongue pushes the drink towards the pharynx then passes the esophagus. The esophageal muscles contract and drive the liquid into the stomach. The stomach muscles contract to stir up the liquid, break it mechanically, and mix it with gastric juice and then pass it to the small intestine little by little. Food in the form of carbohydrates will be digested by amylase pancreas to be disaccharides. The disaccharides are broken down by the disaccharidases into monosaccharides, namely the glucose. This glucose absorption occurs in intestinal absorption. After being absorbed by the villi of the small intestine, glucose, watersoluble vitamins, amino acids, and minerals will then be carried by blood vessels and circulated throughout the body, including muscles that are actively contracting like the uterine muscles during delivery process.<sup>1,8</sup> In other words, glucose is the primary fuel for muscle contractions.<sup>17</sup>

The mean frequency and duration of uterine contractions during the first active stage in the treatment group were higher than the control group, and statistics showed significant differences between the two groups. There was also a considerable difference between the treatment and the control group concerning contraction intensity. The results showed the success of giving mixed-fruit juice beverages. The high carbohydrates contained in the mixed-fruit juice beverages, which were equal to 83 kcal/hour that could be a source of nutrition and the primary source of energy for myometrial contraction.<sup>2,7</sup>

Muscle during contractions strenuous activities are highly dependent on the availability of carbohydrates as energy because of the ability of the muscles to use fat as limited energy. If the availability of glucose is lacking, it will cause lactic acid to accumulate, which will cause the pH blood and muscles to decrease, the work of glycolytic enzymes inhibited, disrupt chemical reactions in muscle cells, and inhibit the release of Ca2+ ions and eventually cause impaired muscle contraction. Therefore, for doing endless activities for more than one hour, it is recommended to increase the absorption of glucose from outside in addition to relying on reserves from the body.18

A proper contraction will affect the progress of the delivery process. Rahmani et al.'s9 study found that low-risk women with 3-4 cm cervical dilatation with the intake of dates or orange juice during the active delivery process could reduce the duration of the second stage of the delivery process. The uterine contractions occur in the dynamic segment that causes the uterine retraction and fetal pushing to the bottom of the pelvis. Retraction and the moving down of fetal head cause the stretching of the lower uterine segment, thinning and opening of the cervix. Regular uterine smooth muscle contractions result in progressive thinning and widening of the uterus which can affect the progress of the delivery process. Myometrial contractions continue to increase with the development of the delivery process due to a positive feedback cycle involving oxytocin and prostaglandin. Oxytocin is a peptide secreted by the posterior pituitary which can change transmembrane ion currents in myometrial smooth muscle cells to produce uterine contractions continuously.<sup>19</sup>

In this study, the phytochemical content from each mixed-fruit juice ingredients was not examined. Hence it could not be explained in detail. Therefore, further research is required to explore the effect of the phytochemical content of mix juice ingredients on the progress of the delivery process, especially on uterine contractions and cervical dilatation.

#### Conclusion

Mixed-fruit juice beverages during the delivery process can affect uterine contractions and cervical dilatation during the active stage of the delivery process.

#### **Conflict of Interest**

All authors declare that there was no conflict of interest in this article.

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#### **RESEARCH ARTICLE**

#### Community Knowledge and Behavior in the Utilization of Medicinal Plants in Cikoneng Village Bandung District

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#### Abstract

The industry of the traditional medicinal made from medicinal plants was currently growing. Effortless cultivation and utilization of medicinal plants were an important step to preserve the traditional medicine of Indonesia. Cikoneng village had abundant natural potential and is an assisted village of the researchers' institution located at the foot of Manglayang mountain Bandung district. Therefore, the researchers implemented the intervention program to educate and socialize the use of medicinal plants to the community of Cikoneng village. After the intervention program, the assessment of the level of knowledge and perceptions of people in the behavior of treatment by medicinal plants utilized was carried out. This study aims to assess the increase in knowledge and perceptions of people in the behavior of cultivation and treatment by using medicinal plants in Cikoneng village. The study used an intervention program and questionnaire with 35 respondents conducted on 22 August–23 September 2016. The results showed that after the intervention program, the level of knowledge of the Cikoneng village community regarding medicinal plants was right. The entire people of Cikoneng village is willing to take advantage of medicinal plants in maintaining family health and will begin to cultivate them in the smallest scope (family). In conclusion, there is an increase in people's knowledge and perception of cultivation and treatment by utilizing medicinal plants in Cikoneng village.

Key words: Behavioral, Cikoneng village, community, herbal medicine, knowledge, perception

#### Pengetahuan dan Perilaku Masyarakat dalam Pemanfaatan Tanaman Obat di Kampung Cikoneng Kabupaten Bandung

#### Abstrak

Industri obat tradisional berbahan baku tanaman obat saat ini semakin berkembang. Upaya budidaya dan pemanfaatan tanaman obat yang optimal merupakan langkah penting untuk menjaga kelestarian obat tradisional Indonesia. Kampung Cikoneng mempunyai potensi alam yang melimpah dan merupakan desa binaan institusi peneliti yang terletak di kaki Gunung Manglayang Kabupaten Bandung. Oleh karena itu, peneliti melaksanakan program intervensi untuk mengedukasi dan menyosialisasikan pemanfaatan tanaman obat kepada masyarakat Kampung Cikoneng. Pada akhir program intervensi, dilakukan penilaian tingkat pengetahuan dan persepsi masyarakat tentang perilaku pengobatan dengan tanaman obat. Penelitian ini bertujuan menilai peningkatan pengetahuan dan persepsi masyarakat tentang perilaku budidaya dan pengobatan dengan memanfaatkan tanaman obat di Kampung Cikoneng. Penelitian menggunakan program intervensi dan kuesioner dengan jumlah responden 35 orang yang dilaksanakan pada 22 Agustus–23 September 2016. Hasil memperlihatkan bahwa setelah program intervensi, tingkat pengetahuan masyarakat Kampung Cikoneng memanfaatkan tanaman obat dalam menjaga kesehatan keluarga dan akan mulai membudidayakannya dalam lingkup yang paling kecil (keluarga). Simpulan, terdapat peningkatan pengetahuan dan persepsi masyarakat tentang perilaku pengobatan dengan memanfaatkan tanaman obat di Kampung Cikoneng.

Kata kunci: Kampung Cikoneng, masyarakat, pengetahuan, perilaku, persepsi, tanaman obat

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#### Introduction

Indonesia has many sources of plants and natural ingredients which use as medicinal plants. The use of medicinal plants started for thousands of years ago, but its utilization has not been optimal. Often raw materials from Indonesia cannot be used in their own country, so these raw materials exported abroad and after being commercialized by outside parties are then returned to Indonesia. Indonesian medicinal plants should be able to host their own country.<sup>1,2</sup>

The current government has promoted various programs related to efforts to improve the health of the community through the use of medicinal plants, including the program of family medicinal plants/*tanaman obat keluarga* (TOGA) and scientific certification of herbs.<sup>3–5</sup> Family medicinal plants are a program for the community related to the utilization of yield crops home-based cultivation that is efficacious as a medicine. This program is beneficial and efficient because in its implementation because it requires less extensive land, such as in the yard, garden or fields that can be used to cultivate plants that are efficacious as medicine in order to meet the family's need for medicines.

At present, the government is also promoting the use of traditional medicines in health through herbal medicine certification. The government wants the use of herbal medicine in the community to increase with the support of authorized health personnel. The use of traditional medicine itself used as a preventive, curative and complementary effort with modern medicine.<sup>3–5</sup> Empowerment of medicinal plants in the community is not only a government program, but also requires the support of educational institutions, drug companies and the community itself to support success the program. The use of medicinal plants in the community needs to be revived for various aspects so that the results will be optimal.

The researchers' institution has several built regions/villages, one of which is Cikoneng village (Cibiru Wetan village, Cibiru Wetan subdistrict, Bandung district). The village enormous agricultural potential with geographical conditions and a very supportive climate. The area of Cikoneng village located at the foot of Manglayang mountain, which is mostly in the form of highlands (hills), while a small portion is in the form of lowlands and dominated by rice fields. The area is suitable for farming because in addition to fertile land, climate and elevation, and abundant water availability.

Based on the description above, the researcher will play an active role in helping the people of Cikoneng village to improve their health status, through increasing their knowledge of the community regarding the use of medicinal plants. This service activity is expected to provide insight into the importance of medicinal plants, how to use them and equip them with the necessary skills in making herbal plants. The use of this medicinal plant use as a preventive, curative, and rehabilitative effort in improving the health status of the family. Following the government program as well, in addition to the utilization of medicinal plants, the community is expected to increase knowledge about medicinal plant and perception level in seeking behavioral level to the utilization of herbal medicine at the Cikoneng village community.

#### Methods

This intervention program for the education of the community, involving the assisted villagers. The target of the intervention program is the residents of Cikoneng village, Cibiru Wetan sub-district, Bandung district, West Java province. This location chose because Cikoneng village is one of the village areas fostered by the researchers' institution. Its location, which is relatively far from the center of government and the city center, makes the majority of its residents prefer daily activities as laborers, farmers, farm laborers, farmers around their homes.

The inclusion criteria stipulated in this program are as follows residents of Cikoneng village, consists of farmers/farm laborers, integrated service center/*pos pelayanan terpadu* (posyandu) and family welfare education/ *pendidikan kesejahteraan keluarga* (PKK) members as activators of the program to use medicinal plants, and are willing to participate in this activity.

This program is a continuous and directed activity involving residents, posyandu cadres in Cikoneng village, and the Bandung District Agriculture Office. This program is planned to be carried out in three stages of activity or three periods of activity. The first period is education and program socialization, the second period is land use/planting postharvest medicinal plants and the third period are an establishment of *Rumah Jamu Kampung* (RUJAK) Cikoneng and establishment of *Komunitas Pintar Obat Herbal* 

#### (KOMPOR) Cikoneng.

The first period of the intervention program was held in the period 22 August to 23 September 2016, which divided into two stages of activity, the preparation and implementation stages. The preparation phase includes the activities of survey to analyze the situation and prepare for the implementation of activities. Support from the government and local authorities must also be fostered from the start because it is one of the factors that will determine the success of the program.

Educational materials provided to the community consisted of Module 1: Community empowerment in utilizing and cultivating herbal plants and Module 2: Practices in making simple herbal preparation and cultivation of medicinal plants.

At Module 1, the material provided is the introduction of traditional medicine, the role of medicinal plants in improving health status, and the introduction of types of medicinal plants that have been widely used empirically and based on scientific research. This module also contains ways to grow medicinal plants ginger, turmeric, and *temulawak*. This type of plants chosen because its efficacy was proven empirically and scientifically, its availability is easy, economical, and its cultivation is not difficult.<sup>6-10</sup>

Module 2 contains the practice of making simple herbal preparations and cultivation of medicinal plant ginger, turmeric, and *temulawak*. Herbs preparations introduced to the public are the method of making infusions, decoctions, and herbal tea. The cultivation of medicinal plants is carried out on a micro scale, which is planting in a field of around.<sup>6-10</sup>

The final stage of the intervention program, knowledge and awareness of the community or residents regarding the cultivation of medicinal plants and their utilization will be assessed using a questionnaire, to see how the results of the socialization and program implementation. The questionnaire consisted of 30 item questions, divided become 15 items for assessing knowledge level and 15 items for assessing perception level in seeking behavior-every question consisting of one correct answer and two distractors. Assessments were graded o for the wrong answer and 5 for correct, and complete assessments graded into three categories. Good categories (value>30), adequate/enough ratings (grades 15-30) and poor ratings (<15).

Devotion to the Cikoneng village community

is carried out based on the planned design so that the final goal is achieved. The indicators were used to assess the success of the implementation of this program are the knowledge and perception level in seeking behavioral to the utilization of herbal medicine at the community of Cikoneng village Bandung regency.

This intervention program approved by the Health Research Ethics Committee of Faculty of Medicine, Universitas Islam Bandung by ethics approval letter number: 375/Komite Etik.FK/IX/2016.

#### Results

At the end of the intervention program, the questionnaire regarding the medicinal plants and their use was carried out. The number of participants who were willing to fill out the questionnaire were 35 people with the characteristics as shown in Table 1.

Assessment of the level of knowledge of the community before the training was conducted qualitatively with discussion followed by question and answer session (Table 2).

#### Discussion

Herbal medicine is currently increasingly being used in the community as one of the primary treatment alternatives to improve health.<sup>1,5</sup> The national health system shows data that household access that can provide health service facilities in remote areas is still low and expensive health services lead to low public accessibility to health services. This reinforces the need for the existence of this program to increase public knowledge about herbal medicine as an alternative treatment, so it is expected that the number of people seeking self-treatment will increase.<sup>11–13</sup>

Evaluation at the end of the intervention program, the questionnaire was taken regarding participants characteristics and knowledge about medicinal plants and their use. This study shows that most participants are female because they had more free time than male. Most of the male in Cikoneng village are farmers or gardeners. From Table 1, what is quite concerning is the education data and family income per month. Public education, in general, is still low, although for the younger generation it has begun to step on further education. Only one person has a diploma in education. Family income is still relatively low,

Characteristics —	Parti	cipants
	Male	Female
Age (year)		
≤17	_	4
18-50	5	-
>50	-	26
Status		
Married	5	4
No married	_	26
Occupations		
Housewife	_	20
Laborer	1	_
Farmer/gardener	4	5
Pre-elementary teacher	_	1
Unemployment	-	4
Last education		
No school	1	_
Primary school	2	12
Secondary school	2	11
Senior high school (SHS)	_	5
Unfinished SHS	-	1
Diploma	—	1
University	—	-
Number of children		
0	-	5
1	2	10
2	1	8
3	1	4
>3	1	3
Aonthly income		
No income	-	4
≤Rp200,000.00	-	5
Rp200,000.00-Rp1,000,000.00	4	18
≥Rp1,000,000.00	1	3
Blank data	—	_

with a large number of family members causing income to become increasingly inappropriate. Economic problems still seem to be one of the problems in this village, even though the location of this village is not too far from urban areas. Many opportunities can be developed in this village, including one that seeks the use of surrounding land for cultivation of herbs. The cultivation of herbal plants is expected to be a good enough commodity to improve the economic conditions

 Table 2 Knowledge and Perception Levels in the Utilization and Cultivation of Medicinal Plants in the Cikoneng Village

Parameters Assessed		Category (%)	
Parameters Assessed	Good	Enough	Poor
Knowledge level	80	20	0
Perception level in seeking behavioral to utilization of herbal medicine	100	0	0

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of the people in Cikoneng village.10,11

The questionnaire to participants looked at the level of community knowledge about herbal medicine before and after training and looked at their perceptions about the future use of medicinal plants or their treatment behavior in using medicinal plants. Questionnaire filling before training is complicated because the time is limited and conditions on the ground are not possible.<sup>12-14</sup>

Assessment of the level of knowledge of the community before the training was conducted qualitatively with discussion and question and answer with the participants present. The results illustrate that in general, they have heard about medicinal plants and their efficacy for health, but only superficially. They do not know much about the advantages and disadvantages of using medicinal plants in maintaining health, what are the types of medicinal plants and how they used. After training the level of community knowledge about medicinal plants, the efficacy and how to use medicinal plants is relatively increasing.

This study showed that after training the community has a right level of knowledge (80%) and perception level in seeking behavioral the utilization of herbal medicine (100%). The results are outstanding when compared with the Hilal and Hilal<sup>14</sup> study, which shows data that the level of knowledge of herbal medicines of the participating physicians (64.6%). In contrast, there were only two out of 96 participants (2.1%) having an advanced level of knowledge of herbal medicines. Other studies that assessed the level of knowledge about herbal medicine for students in Bahrain showed that more than 50% of respondents believed that herbal medicines were effective and should be integrated into the modern health care system.<sup>15</sup> The research by Kashani et al.16 showed that 47.3% of participants from infertility patient in care center were knowledgeable of herbal remedies, with female gender and lower educational background being the associated factors in knowledge.

The healthy behavior of the community is very closely related to the comprehensive patient handling cycle, which starts from preventive, curative, rehabilitative and promotive. In each phase, the community is expected to have good behavior so that eventually it will improve health. When a person faced with a sick or unhealthy condition, some people look for modern medicine that is closely related to chemical drugs, while others seek traditional medicine such as using herbal medicines. The community must understand the concept of traditional medicine with medicinal plants (herbal medicine) correctly. In principle, medicinal plants allow it to develop so that the types and herbal preparations available can vary, and their use is optimal.<sup>4–10</sup>

Good knowledge shall increase individual attitudes to be more positive about using herbal medicines. Study of Hilal and Hilal,<sup>14</sup> it was seen that almost all physicians in participants had never used herbal medicines. Research in Bahrain showed about 70% of the students surveyed had used at least one form of herbal therapy.<sup>15</sup> Another study in Kenya involving 167 patients at a herbal clinic in the Gucha district showed that 68.9% preferred using herbal medicines.<sup>17</sup> In this study, participants showed a desire to use herbal medicine as much as 100%. These results prove that the program intervention carried out has given participants good experience and knowledge about medicinal plants.

#### Conclusion

There is an increase in people's knowledge and perception of the behavior of cultivation and treatment by utilizing medicinal plants in Cikoneng village.

#### **Conflict of Interest**

All authors have not conflict of interest in publishing this article.

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#### **RESEARCH ARTICLE**

#### Effectiveness of Various Mosquito Attractant Solutions to Control Mosquito Population

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#### Abstract

The vector-borne disease is a disease caused by an organism that can transmit disease between human or animal to human. In Indonesia, several vector-borne diseases are a burden of the government including dengue fever, chikungunya, filariasis, and malaria. The attractive baited lethal ovitrap (ALOT) is a novel strategy to alleviate mosquito populations in three main actions: attraction, an adulticide, and larvacide. Research using plant infusion can attract mosquitoes to lay their eggs is needed. This study aims to compare the effectiveness of the mosquito repellent solution using materials from organic waste in Bandung. This study was a quantitative analytic study with a quasi-experimental design conducted in the Faculty of Medicine Universitas Padjadjaran area in October 2016–July 2017. Research subjects are mosquito eggs in a solution which placed at 25 different places for every solution. The analysis was performed using Kruskal-Wallis test followed by the Dunn test. The result of the Kruskal-Wallis test indicates the difference of effectiveness of each solution (p<0.05). Based on the results of the Dunn test, the most significant difference found in the solution of wood shavings with the vegetable waste solution and the solution of wood shavings with corn straw (p<0.05). In conclusion, there is a difference in the effectiveness of the mosquito.

Key words: Effectiveness, mosquito population, mosquito attractant solution

#### Efektivitas Berbagai Larutan Penarik Nyamuk untuk Mengontrol Populasi Nyamuk

#### Abstrak

Penyakit tular vektor adalah penyakit yang disebabkan oleh organisme yang dapat mentransmisikan penyakit antarmanusia atau hewan ke manusia. Di Indonesia, terdapat beberapa penyakit tular vektor yang masih menjadi beban pemerintah, di antaranya demam berdarah, *chikungunya*, penyakit kaki gajah, dan malaria. *Attractive baited lethal ovitrap* (ALOT) merupakan strategi baru untuk menurunkan populasi nyamuk dalam tiga aksi utama, yaitu *attraction, adulticide*, dan *larvacide*. Penelitian terkait larutan dari tanaman yang dapat menarik nyamuk sangat diperlukan. Penelitian ini bertujuan membandingkan efektivitas larutan penarik nyamuk dengan menggunakan bahan dari limbah organik yang ada di Kota Bandung. Penelitian ini adalah penelitian analitik kuantitatif dengan desain quasi-eksperimental yang dilakukan di lingkungan Fakultas Kedokteran Universitas Padjadjaran pada bulan Oktober 2016–Juli 2017. Subjek penelitian merupakan telur nyamuk yang ada pada larutan yang diletakkan pada 25 titik untuk setiap larutan. Analisis dengan Uji Kruskal-Wallis yang dilanjutkan dengan Uji Dunn. Hasil penelitian dengan Uji Kruskal-Wallis menunjukkan perbedaan efektivitas tiap-tiap larutan (p<0,05). Berdasar atas hasil Uji Dunn, perbedaan yang paling signifikan terdapat pada larutan serutan kayu dengan larutan sampah sayur dan larutan serutan kayu dengan jerami jagung (p<0,05). Simpulan, terdapat perbedaan efektivitas larutan penarik nyamuk dan larutan yang menarik nyamuk paling banyak untuk bertelur adalah larutan jerami jagung.

Kata kunci: Efektivitas, larutan penarik nyamuk, populasi nyamuk

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#### Introduction

The vector-borne disease is a disease caused by a microorganism on the human population. Vector is a living organism that can transmit disease from human or animal to human.<sup>1</sup> Mosquito is one of the prominent vectors besides fly, flea, and some aquatic snails.<sup>2</sup> In Indonesia, there are four major diseases transmitted by a mosquito, that is dengue, chikungunya, filariasis, and malaria.<sup>3.4</sup>

Several attempts on vector control have been made such as diminishing resources (eliminate any the container capable of the storing water), larviciding (temephos, Bacillus thuringiensis), biologic control (mosquito-eating fish), and the adulticiding (room spray, insecticide-treated nets, lethal ovitrap as well as autocidal ovitrap). The attractive baited lethal ovitrap (ALOT) is a novel strategy that is designed to alleviate mosquito populations in three main actions: 1) attraction; 2) adulticide; 3) larvacide. Study regarding the effectiveness of organic solution based attractant studied various times, some of which are using the hay infusion,<sup>5</sup> grass infusion,<sup>6</sup> chicken manure infusion,7 guava leaves and potato skin infusion,8 and oak leaves infusion.9 The research using plant infusion can enhance egg excretion by mosquitoes.<sup>10</sup> However, a study regarding the most effective attractant using organic waste from Bandung city and Sumedang regency have not done. Therefore, this study was conducted to determine the most effective solution to attract the mosquitoes as one of the autocidal ovitrap components that will distribute to the community as an attempt to control the mosquito population to decrease the incidence of mosquito-borne disease.

#### Methods

This study is a quantitative analytic study with a quasi-experimental design conducted in the Faculty of Medicine Universitas Padjadjaran area in October 2016–July 2017. Research subjects are mosquito eggs in a solution which placed at 25 different places for every solution. Ovitrap placed on region conserved from the rainwater. This study has got permission from the Faculty of Medicine Universitas Padjadjaran and ethical approval from the Health Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran with letter number: 382/UN6.C.10/ PN/2017.

Making a solution begins with drying the

ingredients until parched. Components utilized are the corn straw, rice straw, wood shavings, vegetable waste (Chinese cabbage), fruit waste (guava, melon skin, watermelon skin, and jicama skin), weed, and water hyacinth. Those materials used because easily found as organic waste in the community. Parched ingredients were put inside a bucket containing tap water with a ratio of 500 grams in 120-liter water, closed tightly, then left for seven days. After seven days, the solution filtered.<sup>11</sup>

The study begins with putting the filtered solution into a 1.5-liter black container which patched with filter paper surfacing the inside area of the container. Each container comprising different solution placed in 13 regions outside room and 12 areas inside the room due to limited active rooms used as depicted in Figure, then ovitrap was left for seven days. After that, the whole eggs found calculated. The data analyzed with the Kruskal-Wallis test and proceed with the Dunn test.

#### Results

Data obtained from the calculation of the number of eggs contained in each solution is in Table 1. Based on the data, the least amount of eggs found in ovitrap placed in the parasitology laboratory room. The most number of eggs found in ovitrap placed in the hallway of buildings C1 and C4.

Results of data analysis using the Kruskal-Wallis test showed a significant difference in the number of eggs found in each solution (p<0.05). The tested solution can be sorted based on its effectiveness in attracting the mosquitoes to lay eggs. In Table 2, it can see that the most effective solution for attracting mosquitoes is a solution made from corn straw.

Results of the Kruskal-Wallis test showed a significant difference, and then the data analyzed with the Dunn test to compare the two solutions and see whether the differences between the two solutions were significantly or not. Dunn test results were in Table 3. The Dunn test results showed that there were significant differences (p<0.05), namely the solution of wood shavings compared to vegetable waste, and corn straw.

#### Discussion

Results of egg calculation in this study indicate a difference in the number of eggs found in each solution. Several factors influence this difference

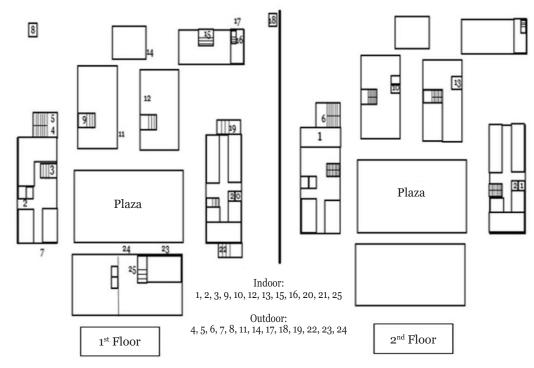


Figure Ovitrap Placement Layout

Table 1 Density of Eggs on Each	Solution
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NT-	DI	Solution Types						
NO.	Place	Fruit	Vegetable	Wood	Grass	Corn	Rice	Water Hyacinth
1	Parasites Lab.	0	0	1	2	1	4	0
2	Front of toilet C4	1	3	1	5	2	2	3
3	Under stairs in building C4	1	1	0	5	5	5	0
4	Under stairs outside building C4	4	5	4	5	5	3	5
5	1 <sup>st</sup> -floor stairs outside building C4	2	2	0	1	3	4	1
6	2 <sup>nd</sup> -floor stairs outside building C4	1	4	1	4	4	4	1
7	Hallway C4.1	5	5	5	5	5	5	5
8	Security post C5	5	5	2	5	5	4	2
9	Under stairs in building C5.1	3	5	1	0	5	2	0
10	Men's toilet in C5.2	0	3	0	0	1	0	0
11	Hallway C5.1	4	3	4	5	3	5	2
12	1st-floor building C3	5	3	5	3	5	5	3
13	Men's toilet in library	3	5	0	2	4	1	1
14	Household building of FK Unpad*	5	5	2	5	5	5	5
15	Under stairs of <i>musala</i> **	5	5	2	5	5	4	5
16	Stairs C6	1	5	5	2	5	3	2
17	Hallway C6.1	5	5	1	4	5	3	5
18	Security post C6	5	5	4	5	5	5	5
19	Stairs C2	0	5	1	5	5	5	5
20	Men's toilet in 1st-floor of building C2	3	5	5	0	5	5	2
21	Men's toilet in 2 <sup>nd</sup> -floor of building C2	2	0	2	3	3	1	1
22	Hallway C2	5	5	2	2	5	5	5
23	Hallway in front of entrance building C1	5	5	5	5	5	5	4
24	Hallway C1	5	5	5	5	5	5	5
25	In front of men's toilet in building C1	5	5	2	5	5	5	5
	Median	4	5	2	5	5	4	3

\**FK Unpad*: Faculty of Medicine Universitas Padjadjaran; \*\**musala*: prayer room; 0: 1–10, 1: 11–20, 2: 21–30, 3: 31–40, 4: 41–50, 5: >50; numbers in the table can be adjusted accordingly Figure

<b>Type of Solutions</b>	n	Mean Rank
Fruit trash	25	82.32
Vegetable garbage	25	102.70
Wood shavings	25	61.26
Grass	25	90.82
Corn straw	25	109.06
Rice straw	25	94.62
Water hyacinth	25	75.22
Total	175	
p value		0.006

**Table 2 Ranking of Attractants Solution** 

Grass	25	90.82
Corn straw	25	109.06
Rice straw	25	94.62
Water hyacinth	25	75.22
Total	175	
p value		0.006
because female	mosquitoes will	choose and

because female mosquitoes will choose and determine where habitat is possible for larvae to grow, develop and survive visual, tactile, and olfactory stimuli.12 Besides, female mosquitoes determine their spawning grounds physically in terms of the lighting, color, temperature, and humidity and the chemical aspect of an attractant.13

Number of eggs on ovitrap placed in the parasitology laboratory is at least then the point of putting another ovitrap because humans rarely pass the room. Whereas the most trapped eggs found in the hallways of buildings C1 and C4, where there are many human activities. Female mosquitoes need food in the form of blood for the growth of their eggs. The blood required by mosquitoes comes from humans or animals.14,15

Results of data analysis using the Kruskal-Wallis test showed differences in the number of eggs from each solution. The difference in the number of eggs had found in the attractant solution influenced by the composition of the amount and variation of the microorganism population.<sup>16</sup> The use of different solutions will affect the diverse composition of the microorganisms present in the solution. Mosquitoes are attracted to non-volatile chemistry on the surface of the solution detected by the chemotactile mosquito sensory organs. This non-volatile chemical is produced due to the fermentation process of microorganisms and will stimulate mosquitoes to lay eggs.<sup>17</sup> Also, the quality and quantity of substances produced by attractants such as carbon dioxide and ammonia are different so that it will cause a difference in the attractiveness of each solution.18

According to the data obtained in Table 1 can be seen the mean value of each solution. The smallest middle value is in the solution of wood shavings, while the largest is the solution

Comparison	p Value	Result					
B-S	1.000	Not significant					
B-K	1.000	Not significant					
S-K	0.046	Significant					
B-R	1.000	Not significant					
S-R	1.000	Not significant					
K-R	0.606	Not significant					
B-J	0.395	Not significant					
S-J	1.000	Not significant					
K-J	0.008	Significant					
R-J	1.000	Not significant					
B-P	1.000	Not significant					
S-P	1.000	Not significant					
K-P	0.282	Not significant					
R-P	1.000	Not significant					
J-P	1.000	Not significant					
B-E	1.000	Not significant					
S-E	0.881	Not significant					
K-E	1.000	Not significant					
R-E	1.000	Not significant					
J-E	0.255	Not significant					
P-E	1.000	Not significant					
D. furrit trach Corregal	able combage V	sucod ab arring ag					

Table 3 Comparison of Solutions

B: fruit trash, S: vegetable garbage, K: wood shavings, R: grass, J: corn straw, P: rice straw, E: water hyacinth

of vegetable waste, grass, and corn straw. In the Dunn test, the comparison of the solution of wood shavings with grass did not show a significant difference due to the uneven distribution of eggs in the grass solution.

Results of data analysis using the Dunn test showed a significant difference when comparing the solution of wood shavings with corn straw and wood shavings with vegetables. This difference occurs because the distribution of mosquito eggs in containers is uneven. The distribution of eggs in containers influenced by several factors, larvae, and pupae in solution, sun exposure, container size, and container cover. Larvae and nymphs in the solution can produce compounds as attractants that can attract female mosquitoes to lay eggs so those female mosquitoes will lay eggs in containers containing larvae and pupae. Container characteristics, sun exposure, and size have a secondary role.19 The influences of those things minimized using uniform containers and the same placement criteria for ovitrap both indoors and outdoors.

Overall, the Dunn test shows that there is a significant difference in the solution found in this study. The results of this study are not following the research conducted by Sazali et al.<sup>20</sup> In the

study they conducted showed no significant differences in the solution derived from organic materials, namely straw, chili, and palm sugar fermentation.

This study shows that the solution used in this study used as an ovitrap attractant, but several factors influence mosquitoes to put their eggs apart from substances produced from attractants.

Limitation in this study lies in the implementation of research. Researchers are aware of the constraints in this study that ovitrap is not fully awake from other animals such as cats so that the solution can be reduced or spilled.

Further research it is expected to be able to examine the microorganism content that can affect the attractant solution as a practical solution and needs to control external factors that can affect the effectiveness of attractants.

#### Conclusions

Organic ingredients can have used as an attractant for mosquitoes. There is a difference in the effectiveness of each solution as a mosquito pulling solution. The most effective solution is a solution made from corn straw.

#### **Conflict of Interest**

The authors declare no conflict of interest in this study.

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#### **RESEARCH ARTICLE**

#### The Effect of Kerokan to Liver Function of Hepatitis B Patients

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#### Abstract

*Kerokan* is an alternative therapy done by rubbing and pressing the skin surface using oil and a blunt object. This treatment has a hepatoprotective effect as it increases heme oxygenase-1, an essential enzyme in heme catabolism. In hepatitis B, heme oxygenase-1 plays a vital role to fight oxidative stress. Hence the damage on liver cells can be reduced or even prevented. Damaged cells indicate by the production of aspartate aminotransferase (AST/SGOT) and alanine aminotransferase (ALT/SGPT) enzymes that accumulated in the bloodstream. This study aimed to investigate the effect of *kerokan* to liver function by analyzing SGOT and SGPT levels in hepatitis B patients. These were an experimental study with a pre-test post-test control group design conducted in the public health center in Palembang in October 2016. Statistical analysis used the unpaired t test and paired. The research subjects were 30 patients with inactive carrier and chronic hepatitis B. The levels of SGOT and SGPT were determined using the IFCC method. The levels of SGOT in control (19.53±3.44 U/L) and treatment group (20.46±4.53 U/L,  $\Delta$ =0.93) after 24–48 hours were not statistically different (p=0.53). Also, the levels of SGPT in control (18.66±5.40 U/L) and treatment group (19.80±9.25 U/L,  $\Delta$ =1.13) after 24–48 hours were also not statistically different (p=0.68) as well. In conclusion, the liver cells of SGOT and SGPT were still in the normal range.

Key words: Hepatitis B, kerokan, SGOT, SGPT

#### Efek Kerokan terhadap Fungsi Hepar Pasien Hepatitis B

#### Abstrak

Kerokan merupakan terapi alternatif yang dilakukan dengan menggosok dan menekan permukaan kulit menggunakan minyak dan benda tumpul. Pengobatan ini bersifat hepatoprotektif, yaitu meningkatkan produksi enzim *heme oxygenase-1* dalam katabolisme *heme*. Pada hepatitis B, *heme oxygenase-1* berperan penting dalam menangkal radikal bebas sehingga dapat mengurangi atau mencegah kerusakan sel hepar. Kerusakan sel hepar diindikasikan oleh produksi enzim *aspartate aminotransferase* (AST/SGOT) dan *alanine aminotransferase* (ALT/SGPT) yang terakumulasi dalam pembuluh darah. Penelitian ini bertujuan mengetahui pengaruh kerokan pada fungsi hepar dengan mengganalisis kadar SGOT dan SGPT pada pasien hepatitis B. Penelitian meliputi 30 pasien *inactive carrier* dan kronik hepatitis B. Kadar SGOT dan SGPT diukur dengan menggunakan metode IFCC. Kadar SGOT pada kontrol (19,53±3,44 U/L) dan grup perlakuan (20,46±4,53 U/L;  $\Delta$ =0,93) setelah 24–48 jam tidak terdapat perbedaan signifikan (p=0,53). Selain itu, kadar SGPT pada kontrol (18,66±5,40 U/L) dan grup perlakuan (19,80±9,25 U/L;  $\Delta$ =1,13) setelah 24–48 jam tidak menunjukkan perbedaan signifikan (p=0,68). Simpulan, sel hepar pada pasien *inactive carrier* dan kronik hepatitis B tidak mengalami kerusakan setelah terapi kerokan, serta kadar SGOT dan SGPT tetap dalam kondisi normal.

Kata kunci: Hepatitis B, kerokan, SGOT, SGPT

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#### Introduction

Kerokan is a traditional healing therapy used by the people in East Asia using "pressingrubbing" technique. Certain parts of the skin surface are rubbed with oil and pressed by using a blunt object until some of the petechiae appear. Petechiae is an indicator of blood-vessel extravasation in subcutaneous tissues.1 Kerokan has hepatoprotective activity as it activates heme oxygenase-1.2,3 Physical stress on skin cells and blood vessels as a result of kerokan will induce the increased synthesis of heme oxygenase-1.<sup>3,4</sup> Heme oxygenase-1 is a cytoprotective enzyme that catabolizes heme into the biliverdin, carbon monoxide, and ferritin.5 Bilirubin and biliverdin are antioxidants that act as antioxidative stress, but carbon monoxide plays a role in preventing hepatic ischemia and reperfusion injury through the p38 MAP kinase pathway. Meanwhile, ferritin has cytoprotective effects in which it increases the ATPase pump to release Fe<sup>2+</sup> from cytosol.<sup>5,6</sup>

Mechanism of liver cell damage by the hepatitis B virus is initiated by an autoimmune reaction to liver cells infected. Cytotoxic T lymphocyte (CTL) is a specific antibody that damages liver cells infected by hepatitis B virus. The destroyed liver cells lead to necrosis.7 Infection of hepatitis B can be acute and chronic. If virus-eliminating process lasts efficiently, the infection can stop. On the contrary, if the process is less efficient, virus infection will persist. The destruction of liver cells that lasts more than six months is called chronic hepatitis B. Chronic hepatitis B is divided into active-chronic hepatitis B and inactive carrierchronic hepatitis B. In inactive carrier-chronic hepatitis B, the immune response is not sufficient so that necrosis does not occur although virus replication continues to occur.8

Based on the statements mentioned above, the researchers were interested in investigating the effect of *kerokan* on the liver function of hepatitis B patients.

#### Methods

It was an experimental study with a pre-test posttest control group design. Statistical analysis used an unpaired t test and paired.<sup>9</sup> This study conducted on patients coming to the public health centers in Palembang in October 2016. The subject sample size was 30 patients with inactive carrier-chronic hepatitis B, divided into two groups (control had 15 samples and treatment 15 samples). The C control group was without any treatment. The blood sample was taken twice from this group, the first taken in any time based on the circadian clock, and the second took 24–48 hours after the first sample. The samples had sent to the laboratory for serum glutamic oxaloacetic transaminase (SGOT) and serum glutamate-pyruvate transaminase (SGPT) analysis.

On the other hand, the blood samples of the treatment group also collected twice—first, the subjects prepared for blood collection. After the first sample, the subjects exposed to *kerokan* therapy, 24–48 hours after the treatment the blood taken for the second time. In this study, *kerokan* was applied on to whole parts of the back until seen petechiae.<sup>1</sup> The levels of SGOT and SGPT determined by the International Federation of Clinical Chemistry (IFCC) method.

This research has received a permit from the Health Research Ethics Committee of Politeknik Kesehatan Makassar by ethical approval letter number: 297/KEPK-PTKMKS/X/2016.

#### Results

The results of SGOT and SGPT analysis in this study are in Table 1. Table 1 shows that the highest level difference (-3.07 U/L) between the levels of initial SGOT and 24–48 hour SGOT found in the control group. On the other hand, the highest level difference (-2.53 U/L) between the initial SGPT and 24–48 hour SGPT was in the treatment group.

The normality test of SGOT and SGPT levels are in Table 2. The results showed that p value in all groups higher than 0.05 (p>0.05) that means all data in all group normal distributed.

The comparison of SGOT and SGPT levels in the groups by paired t test has described in Table 3. Table 3 showed that p values in both control groups were higher than 0.05 (p>0.05). There was no significant difference in SGOT and SGPT levels between those in the initial and after 24– 48 hours. Table 3 also shows that no significant difference (p=0.00) in SGPT levels among the treatment group with a mean difference of -2.53(U/L).

Table 4 shows a comparison of SGOT and SGPT levels between control and treatment group by unpaired t test. Table 4 reveals that p value in all groups was more than 0.05. Statistically, there was no significant difference between control group and treatment group.

	SGOT			SGPT			
Groups	Initial Mean±SD (U/L)	24–48 Hours Mean±SD (U/L)	Δ (U/L)	Initial Mean±SD (U/L)	24–48 Hours Mean±SD (U/L)	Δ (U/L)	
Control	22.60±5.32	19.53±3.44	-3.07	21.00±6.55	18.66±5.40	-2.34	
Treatment	22.20±6.37	20.46±4.53	-1.74	2233±9.42	$19.80 \pm 9.25$	-2.53	

Table 1 Levels of SGOT and SGPT Analysis

#### Table 2 Normality Test of SGOT and SGPT Levels in Control and Treatment Group

Omerce a	SGOT		SGPT	
Groups	Mean±SD (U/L)	p Value	Mean±SD (U/L)	p Value
Control				
Initial	22.60±5.32	0.92	$21.00 \pm 6.55$	0.83
24–48 hours	$19.53 \pm 3.44$	0.72	18.66±5.40	0.45
Treatment				
Initial	22.20±6.37	0.80	22.33±9.42	0.31
24–48 hours	20.46±4.53	0.67	$19.80 \pm 9.25$	0.17

Normality test with Kolmogorov-Smirnov test p value>0.05

Groups	Initial Mean±SD (U/L)	24–48 Hours Mean±SD (U/L)	Δ (U/L)	p Value
Control SGOT SGPT	$22.60\pm 5.32$ $21.00\pm 6.55$	19.53±3.44 18.66±5.40	-3.07 -2.34	0.69 0.10
Treatment SGOT SGPT	22.20±6.37 22.33±9.42	20.46±4.53 19.80±9.25	-1.74 -2.53	0.22 0.00

Table 3	Comparison	of SGOT	and SGPT Levels
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Paired t test, p value>0.05

#### Discussion

*Kerokan* has hepatoprotective activity as it activates heme oxygenase-1 that plays a vital role to fight oxidative stress.<sup>2,3</sup> SGOT and SGPT could be indicators of *kerokan's* effect on liver function. This present study showed that there was no significant difference (p>0.05) in mean levels of SGOT and SGPT between control group and treatment group both in initial level and after 24–48 hours.

Based on previous studies, the *kerokan* has been proved to have the hepatoprotective effect that increases heme oxygenase-1.<sup>2,5,10</sup> The heme oxygenase-1 itself is a cytoprotective enzyme that catabolizes heme into biliverdin, carbon monoxide, and ferritin.<sup>5</sup> Bilirubin and biliverdin are antioxidants and antioxidative stress. Carbon monoxide prevents ischemia and liver reperfusion injury through the p38 MAP kinase pathway. Meanwhile, ferritin increases the ATPase pump to release Fe<sup>2+</sup> from the cytosol.

According to researchers point of view, the hepatoprotective effect of the heme oxygenase-1 occurs on damaged or injured liver cells (necrosis) as a result of the hepatitis B virus infection. In normal condition, heme oxygenase-1 will remain increased after *kerokan* therapy. The results of

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Concerne a	SGOT			SGPT		
Groups	Mean±SD (U/L)	Δ(U/L)	p Value	Mean±SD (U/L)	Δ(U/L)	p Value
Initial Control Treatment	22.60±5.32 22.20±6.37	-0.4	0.85	21.00±6.55 22.33±9.42	1.33	0.65
24–48 hours Control Treatment	19.53±3.44 20.46±4.53	0.93	0.53	18.66±5.40 19.80±9.25	1.13	0.68

Table 4 Comparison of SGOT and SGPT Levels between Control and Treatment Group

Unpaired t test, p value>0.05

this study were in line with Kwong et al.<sup>3</sup>, who did a similar study on healthy mice. The results showed that heme oxygenase-1 increased after *kerokan* therapy with the highest peak of 36 hours.

Immune response resulting in the damaged liver cells did not occur in patients with inactive carrier-chronic hepatitis B. If the immune response is not active, the necrosis does not occur. However, the virus remains making replication without showing clinical symptoms of damaged liver cells (necrosis). It assumed as an answer of to why no hepatoprotective effect found after *kerokan* therapy on patients with inactive carrierchronic hepatitis B. The results of this study were in line with Chan et al.<sup>11</sup> They proved that there were no significant changes in liver function after *kerokan* therapy was applied.

#### Conclusion

There was no significant difference in the mean levels of SGOT and SGPT between control and treatment group. It possible because the liver cells of inactive carrier and chronic hepatitis B patients were not damaged (necrosis) after *kerokan therapy*, and the levels of SGOT and SGPT were still in the normal range.

#### **Conflict of Interest**

There is no conflict of interest at all authors.

#### Acknowledgments

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## **RESEARCH ARTICLE**

# The Use Reproductive Health Game (KEPO Game) on Female Adolescent's Five Dimensions Satisfaction

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#### Abstract

The adolescent's reproductive health is the major problem that should take into consideration. To solve this problem, it needs an alternative strategy by using a media, reproductive health/*kesehatan reproduksi* (KEPO) game, in Android smartphone. The aim is analyzing the effect of KEPO game on the five dimensions of female adolescent's satisfaction. The research method was quasi-experiment, and the research design used pre-test post-test with control group design. The sampling technique used simple random sampling. The subject was 64 respondents of female student age of 12–15 years old in public junior high school in Bandung city. The respondents divided into two groups, the first one treated by KEPO game is 32 students of Public Junior High School 50 Bandung, while the control group was 32 students of Public Junior High School 8 Bandung, get counseling from Ujungberung Indah Public Health Center; the entire research conducted in April–May 2017. Research result shows the percentage differential of satisfaction average score improvement on both groups. The treatment group produces percentage of content 14.6%, display 23.6%, accuracy 11.4%, easiness 12.4%, and correctness 17%. In the other hand, control group produces content 5%, display 3%, accuracy 4.3%, easiness 2.8%, and correctness 4.7% with a p value for each indicator was p<0.05 on the intervention group and p<0.05 on the control one. Entirely, it known that adolescent's satisfaction from those five aspects in using KEPO game on the five dimensions of female adolescent's satisfaction.

Key words: KEPO game, learning media, satisfaction

# Pengaruh Penggunaan Gim Kesehatan Reproduksi (KEPO) terhadap Lima Dimensi Kepuasan Remaja Perempuan

## Abstrak

Kesehatan reproduksi remaja merupakan masalah utama yang harus diperhatikan sehingga untuk mengatasi ketidakpuasan remaja, diperlukan strategi alternatif, yaitu gim kesehatan reproduksi (KEPO) menggunakan smartphone Android. Tujuan penelitian ini adalah menganalisis pengaruh gim KEPO terhadap lima dimensi kepuasan remaja perempuan. Metode penelitian adalah quasi-experiment dan desain penelitian menggunakan pre-test post-test with control group design. Teknik pengambilan sampel menggunakan simple random sampling. Subjek penelitian adalah 64 responden siswa perempuan usia 12-15 tahun SMP Negeri di Kota Bandung. Responden dibagi menjadi dua kelompok, vaitu kelompok perlakuan menggunakan gim KEPO sebanyak 32 siswa SMP Negeri 50 Bandung, sedangkan kelompok kontrol menerima penyuluhan dari Puskesmas Ujungberung Indah sebanyak 32 siswa SMP Negeri 8 Bandung. Penelitian dilaksanakan pada bulan April-Mei 2017. Hasil penelitian menunjukkan perbedaan persentase peningkatan nilai rerata kepuasan pada kedua kelompok. Kelompok perlakuan menghasilkan persentase konten 14,6%, tampilan 23,6%, akurasi 11,4%, kemudahan 12,4%, dan ketepatan 17%. Di sisi lain, kelompok kontrol menghasilkan konten 5%, tampilan 3%, akurasi 4,3%, kemudahan 2,8%, dan ketepatan 4,7% dengan nilai p untuk setiap indikator sebesar p<0,05 pada kelompok intervensi dan p>0,05 kelompok kontrol. Secara keseluruhan, diketahui bahwa kepuasan remaja dari kelima aspek kepuasan dalam menggunakan gim KEPO memiliki perbedaan yang bermakna p<0,05 dengan persentase puas 84%. Simpulan, terdapat pengaruh penggunaan gim KEPO terhadap lima dimensi kepuasan remaja perempuan.

Kata kunci: Gim KEPO, kepuasan, media pembelajaran

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# Introduction

Human resources become an essential component in reaching health development goal. Qualified human resources are very needed to be able to increase society health status. Furthermore, adolescents have a role as the component of the human resources itself as a precious asset for the nation in the future.<sup>1,2</sup>

According to WHO,<sup>3</sup> the adolescent is a citizen age of 10–19 years, divided early adolescent (10–13 years old), middle adolescent (14–15 years old), and late adolescent (16–19 years old). Next, according to the Regulation of the Minister of Health Republic of Indonesia,<sup>4</sup> adolescent means citizen age of 10–18 years. In the other hand, the National Population and Family Planning Board or *Badan Kependudukan dan Keluarga Berencana Nasional* (BKKBN) says the average age of adolescent is 10–24 years old and unmarried.<sup>5</sup>

Another opinion comes from Mehta et al.<sup>6</sup> said the characteristics of the adolescent are aggressive, dynamic, innovative, overconfident, enthusiastic, explorative, trying something new, sociable, brave, cheerful, and focus in doing something. The whole characteristics had faced with the availability of the surrounding facilities that can fulfill their curiosity. This condition produces the adolescents' conflict somehow. If they choose the incorrect decision in handling their conflict, they may get some continuity risks such as psychosocial and physics problem that even may exist in their lifetime.<sup>5</sup>

Having a special relationship becomes another serious problem that takes attention too. Approximately, it is about 32.1% young female and 36.5% young male age of 15–19 years; they start having a special relationship when they were before 15. If they do not have life skill, they face the risk of possessing an unhealthy relationship.<sup>7</sup>

Reproductive health is one of the other problems of adolescent that needs to take attention to from all parties not only from parents but also from the school counselor. Recently, the adolescents' attitude toward gender reverse has led them to the abnormal attitude of active sex and ignore the right substance in having a real relationship which has a positive role as a place of learning activity, communication, emotion expression, and commitment.<sup>8</sup>

The adolescent based school gain health service through the school health program (*usaha kesehatan sekolah*/UKS). The UKS held Trias UKS consisted of health education, health service, and healthy school environment guidance.<sup>9–11</sup> Adolescent health services that cannot be handled by UKS was served by the public health center (*puskesmas*) that implement young health program (*pelayanan kesehatan peduli remaja*/PKPR).<sup>12</sup> On this research, the selected school is junior high school located in the Puskesmas Ujungberung Indah surrounding.

According to the Government Regulation of Republic of Indonesia Number 61 the Year 2014, reproductive health service had comprised of communication, information, and education.13 The Laws of Republic of Indonesia Number 36 the Year 2009 article 74 says every reproductive health service characterized as promotive, preventive, curative, or rehabilitative with particular attention to peculiar aspects, especially the woman's reproductive health.<sup>14</sup> The teenager's age of 12-15 years in this research has taken from one of UNESCO data that provide topic and learning objectives for teenager age of 12-15 years.<sup>15</sup> Therefore, an learning media of interest had designed based on the technological information.

The development of information technology nowadays has influenced society, especially in the field of game development deals with software development too. One of the mobile smartphone systems that are developing is Android one. Also, it possesses opened character so that it puts a chance for the developers to create their application, especially the game one; it grows fast in the Android system.<sup>16</sup>

Based on the recent study has done in Public Junior High School 35 Bandung, the scenario or instruction in making the game spread out to the students in purpose to know how far the scenario suit the teenagers' need related to adolescent's reproductive health. They said some picture displays look too vulgar, and they suggest to enrich the materials correlate with adolescent's reproductive health.

The degrees of player satisfaction in playing a game is an essential factor in developing the game. Rizkiyani<sup>17</sup> described the evaluation as the process of gathering various information or data to determine the extent, in terms of what, and how the objectives of a program achieved, as well as a systematic process for determining or make decisions to how extent the teaching goals had achieved by the program.

The user's satisfaction or dissatisfaction means a respond in using this education game

Satisfaction Sub-variabel	Gro	- n Valua	
(Scale 100)	Treatment (n=32)	Control (n=32)	- p Value
Content			
Pre-test			
Mean (SD)	71.8 (6.5)	75.1 (9.7)	$0.103^{*}$
Median	68.7	75	0.100
Interval	56.2-81.2	50-93.7	
Post-test			
Mean (SD)	81.8 (4.6)	78.1 (6.9)	$0.011^{*}$
Median Interval	81.2		
	68.7-87.5	62.5-93.7	
Post-test score≥70 (%)	84	47	0.001
Comparison pre-test vs post-test**	<0.001	0.064	0.001
Increase of average (%)	14.6	5	
Display			
Pre-test			
Mean (SD)	70.9 (13.9)	74.6 (10.3)	$0.284^{*}$
Median	75	78	r
Interval	43.7-93.7	56.2-87.5	
Post-test	$\Omega = (\langle c \rangle)$		
Mean (SD) Median	85 (6.9)	76.4 (8.6)	$< 0.001^{*}$
Median	84.4	78	
Interval	68.7–100	62.5-93.7	
Post-test score≥70 (%)	91	50	
Comparison pre-test vs post-test**	<0.001	0.086	<0.001
Increase of average (%)	23.6	3	
Accuracy			
Pre-test			
Mean (SD)	74.4 (6.2)	73.6 (6)	$0.417^{*}$
Median	75	75	0.41/
Interval	50-88	63-88	
Post-test			
Mean (SD)	82.6 (5.2)	76.4 (5.7)	$<0.001^{*}$
Median	81.2	75	<0.001
Interval	68.7–100	68.7-87.5	
Post-test score≥70 (%)	91	28	
Comparison pre-test vs post-test**	<0.001	0.062	0.010
Increase of average (%)	11.4	4.3	
Easiness			
Pre-test			
Mean (SD)	70.3 (6.9)	72 (5.5)	a a(0*
Median	68.7	75	0.068*
Interval	62.5-93.7	62.5-81.2	
Post-test	0,007	Ū.	
Mean (SD)	78.7 (8.2)	73.8 (6.4)	0.010*
Median	81.2	75	0.019*
Interval	68.7-100	62.5-87.5	
Post-test score≥70 (%)	66	22	
Comparison pre-test vs post-test**	<0.001	0.074	0.003
Increase of average (%)	12.4	2.8	
Correctness	·		
Pre-test			
Mean (SD)	74.2 (9)	77.9 (6.3)	
Median		81.2	$0.082^{*}$
Interval	75 56.2–93.7	62.5-87.5	
Post-test	JU-2 JJ-/	02.0 07.0	
Mean (SD)	86 (5)	81 (5.8)	
Median	87.5	81.2	$0.001^{*}$
Interval	75-100	68.7-93.7	
Post-test score≥70 (%)	97	21	0.001
Comparison pre-test vs post-test**	< 0.001	0.074	0.001
Increase of average (%)	17	4.7	

Table 1 Satisfaction Score Before and After Treatment

\*Mann-Whitney test, \*\*Wilcoxon test

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Satisfaction Second	Gro	n Valua	
Satisfaction Score	Treatment (n=32)	Control (n=32)	p Value
Pre-test Mean (SD) Median Interval	72.3 (5.2) 72.5 62.5–86.2	74.7 (4.1) 74.3 66.2–82.5	0.067*
Post-test Mean (SD) Median Interval	82.8 (3.1) 82.5 77.5-93.7	77.1 (3.1) 76.8 71.2-82.5	<0.001*
Post-test score≥70 (%) Comparison pre-test vs post-test** Increase of average (%)	84 <0.001 14.8	25 0.001 3.5	<0.001

\*Mann-Whitney test, \*\*Wilcoxon test

Course of the second se	Satisfa	action	X7-1*	$\mathbf{DD}(\mathbf{OL} \circ \mathbf{-} 0')$	
Groups	Unsatisfied	Satisfied	p Value*	RR (CI 95%)	
Control	24 (75%)	8 (25%)	<0.001		
Treatment	5 (15.6%)	27 (84.4%)	<0.001	4.8 (2.1–11)	
*Chi-quadrat test					

toward the evaluation of disconfirmation, which felt by the user before and after using.<sup>18</sup> Education game as a learning medium completed by a fascinating visualization; has a purpose of facilitating the user in getting the given information quickly. An educational game as a learning media with interesting visualization so that users can easily find out the information conveyed. The function of this educational game is as a media of communication or the delivery of information through digital media and is informal so it must fulfill five dimensions of satisfaction; there are content, display, accuracy, easiness, and correctness.<sup>19</sup>

Based on the statements mentioned above, it needs an alternative strategy by using a media, the reproductive health/*kesehatan reproduksi* (KEPO) game, in the Android smartphone. This study aim was analyzing the effect of KEPO game on the five dimensions of female adolescent's satisfaction.

# Methods

This research used a quasi-experiment method completed using pre-test post-test with control

group design. Two groups analyzed, the treatment and the control group. The treatment group is measured before and after KEPO game giving for a month, then evaluated every once a week. In the other hand, the control one is measured before and after the regular program of PKPR/UKS giving. The target population in this research were female student age of 12-15 years in the public junior high school in Bandung. The whole research had done in Public Junior High School 50 Bandung for the treatment group and Public Junior High School 8 Bandung for the control one. The reached populations are female students class 8 age of 12-15 years in Public Junior High School 8 Bandung as the control group and Public Junior High School 50 Bandung as the treatment group that fulfills the inclusion and unfulfilled the inclusion criteria. Next, the sample taking technique in this research is simple random sampling in a simple random way from each student pull the lottery and exit the lottery number according to pull the lottery, with 32 students of treatment group and 32 students of control group that fulfill the inclusion criteria and not include the exclusion criteria, so the total population are 64 people.

The inclusion criteria are young age of 12–15 years class 8 of public junior high school, have smartphone android based with minimum 1 gigabytes (GB) of random-access memory (RAM) and able to use it; can install the KEPO game. They play the game frequency minimum three times a week in 60 minutes per day. The students who willing to be respondents get the treatment of game usage, from public junior high school which has inactive PKPR/UKS program, Public Junior High School 50 Bandung. Next, the control group got a counseling program that has run well, PKPR/UKS, Public Junior High School 8 Bandung. Whereas the exclusion criteria, the sick students, the absence student in pre-test and post-test, the adolescent who has experienced formal reproductive health education. Finally, drop out calls for the adolescent who never apply the KEPO game three times a week.

This research is the use of educational tools in the form of games and has gone through stages of development that ensure reliability. In the treatment, the group played the KEPO game for one month and evaluated once a week to junior high school, then post-test. The control group was given PKPR program counseling from Puskesmas Ujungberung Indah through UKS, then one month later a post-test was conducted. The grace period of the study was one month, based on the results of research on time satisfaction was able to determine customer satisfaction with a variable. Data analyzed by chi-square test, Wilcoxon test, and Mann-Whitney test.

This research applies the three principles of the Belmont Report: respect for person, beneficence, and justice. Also, this research had approved by the Health Research Ethics Committee of the Faculty of Medicine of the Universitas Padjadjaran Bandung by ethical approval letter number: 285/UN6.C.10/PN/2017.

# Results

Table 1 showed that satisfaction score (content, display, accuracy, easiness, and correctness) on the pre-test both groups shows there is no difference; based on Mann-Whitney test result has p value>0.05, that means both groups are comparable. The pre-test and the post-test result shows a meaningful comparison based on the Wilcoxon test, p value<0.001. Based on this data, there is a difference in satisfaction score before and after treatment with p value<0.001 increase.

The research result from Table 2 shows different calculation score of pre-test and posttest on both groups increased. Wilcoxon test on the treatment group produces satisfaction score improvement after pre-test and post-test giving with the result p value<0.001. In line with the treatment one, the score increase on both groups, the percentage increase and get higher on the treatment one 14.8%, while the control group only produce 3.5%.

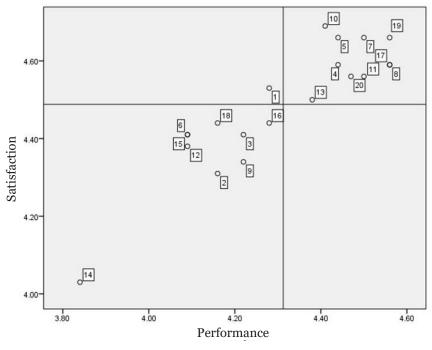
Based on Table 3, the usage of the KEPO game interferes adolescent satisfaction with p value<0.001. Relative risk (RR) score was 4.8, that means the respondent who did not apply the game probably get risk 4.8 times to feel unsatisfied than the game user one.

## Discussion

The usage of KEPO game interferes the adolescent satisfaction reflected by game content dimension. Table 1 shows the difference exists to the content satisfaction improvement before and after game using, p value<0.001. Improvement percentage of satisfaction content average on both groups increased: the treatment group 24.6% and the control one only 5%. Statistically, it shows a different satisfaction content score on both groups reflected by p value=0.011. It is suitable with previous research by Green and Pearson,<sup>20</sup> tells content gives positive influence to the application user. As consideration for further development planning, the management expected to be able to consider more the application content.<sup>21</sup> Next, the interactivity includes the ability to set display, nuances, and content gives interaction to the user.20

The use of KEPO game influences adolescent satisfaction based on the game display dimension. The display dimension measures the user's satisfaction viewed by the application display. The total value from a game centered on design and time duration. Education game application organized with new and interactive design. The time duration determination in this game applies the timer feature.<sup>18,20</sup> The display format or information which is produced by application system needs to decide whether it is exciting or not, and how the display works whether the system works well to ease the user in gaining core information on its application or not.<sup>22</sup>

Table 1 shows there was a difference in display satisfaction enhancement before and after KEPO



**Figure Cartesius Diagram** 

game using, with p value<0.001. The percentage of the increasing average of display satisfaction on both groups get enhancement; the treatment group is 23.6%, and the control group only get 3%. Statistically, it reflects the difference of the content satisfaction value between both groups, which showed by p value<0.001.

Another influence of KEPO game usage on adolescent satisfaction was from game accuracy. On this research, it shows the difference of accuracy satisfaction enhancement before and after game using with p value<0.001. The percentage of the increasing average of accuracy satisfaction on both groups get enhancement; the treatment group was 11.4%, and control one only got 4.3%. Statistically, it reflects the difference of accuracy satisfaction value between both groups, which showed by p value<0.001.

According to Mosley,<sup>23</sup> there are two methods for accurately measuring satisfaction, namely the product definition of the application system and the identification of attributes of relevance that are indicators of the key to effectiveness. Moreover, the quality of the application system can give any influence to the user satisfaction. The better the application system quality, the better the user satisfaction will be. Decision taking to answer the question in the game has given to the user.24

Also, KEPO game usage interferes the adolescent satisfaction viewed by the game easiness dimension. Useable and accessible become a crucial point that needs to exist in an information system, and it tries to organized with interface way which is user-friendly so that it expected for the user could be able to use the game application easily.<sup>19</sup>

Table 1 reflects the existent of difference in easiness satisfaction enhancement before and after game using with p value<0.001. The percentage of the increasing average of easiness satisfaction on both groups reach enhancement; the treatment group was 12.4%, yet control one only gets 2.8%. Statistically, it reflects the difference of easiness satisfaction value between both groups that showed by p value<0.019.

It correlates with Sutanto's<sup>22</sup> research that easiness can be categorized well because the user has a strong relationship between satisfaction and the easy of the game using. The Table of Estimation Parameter Regression Weights showed the relation of satisfaction and easiness conclude the estimation result was 0.806, means the better the easiness felt, the higher the satisfaction felt will be.

Finally, it discussed the use of KEPO games

from another point of view, namely the game correctness dimension. Correctness means the following information to the receiver well received and on time; the information must be up to date too. The old information is not precious anymore since the information is a base decision in decision making.<sup>20,25</sup>

Table 1 shows the existent of difference in correctness satisfaction enhancement before and after game using with p value<0.001. The percentage of the increasing average of correctness satisfaction on both groups reach enhancement; the treatment group was 17%, yet control one only gets 4.7%. Statistically, it reflects the difference of correctness satisfaction value between both groups that showed by p value=0.001. Also, in line with Sutanto's<sup>22</sup> research tells correctness is categorized well since the user who applies the application get time efficiency.

The level of adolescent satisfaction with the KEPO game shown in the Cartesian diagram (Figure). Quadrant A is the main priority. The component that includes quadrant A and as improvement priority is item number 1, related to information in learning media. Quadrant B is keep the achievement. The components of this quadrant are item number 4 (animation picture), 5 (learning media display design), 7 (suitability of picture and material), 8 (color selection on learning media), 10 (detail of information given), 11 (positivity of information given), 13 (use understandable language), 17 (well-received information given), 19 (up to date information), 20 (correctness of font size, color, and font type).

Quadrant C is low priority. The components of this quadrant are item number 2 (variety exciting information), 3 (readable and understandable text), 6 (interactive), 9 (clarity of material goal), 12 (suitability of information with learning goal), 14 (easiness to accesses adolescent reproductive health), 15 (clarity of material presentation), 16 (easiness to comprehend adolescent reproductive health theory), 18 (suitability of age and material). Quadrant D is extremely. There is no component on this quadrant.

Satisfaction scores on the dimensions of content, display, accuracy, easiness, and correctness in both groups before and after the treatment had a significant percentage of satisfaction in the treatment group (84%). The increase in satisfaction scores in both groups showed RR=4.8, which means respondents who did not use the KEPO game had a 4.8-fold risk of dissatisfaction compared to respondents who used.

#### Conclusion

There was an effect of KEPO game on the five dimensions of female adolescent's satisfaction.

## **Conflict of Interest**

The authors declare no conflict of interests.

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#### **RESEARCH ARTICLE**

# Prescription Writing Errors in Clinical Clerkship among Medical Students

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#### Abstract

Prescription is an instruction written by a medical practitioner to give a drug or device for a patient. The proper prescription will contribute to speedy recovery or healing process for the patient. Clinical clerkship must have an excellent competency to choose the right medication and prescribe the appropriate drugs or therapy. This study aims to analyze the common error in prescription's writing in clinical clerkship among medical students at their final examination to be a medical doctor. This study used the analytic method to 609 sheets of prescription from 180 clerkship students in their last try out on objective structured clinical examination (OSCE) at the Faculty of Medicine Universitas Islam Bandung in March 2018. Analyzed the component that every prescription should have, which consists of patient identity, superscription, inscription, subscription, and signatures. The result showed that more than half of the clerkship students made an error in subscription (50.25%) and signatures items (55.83%), while most of them had written down properly the patient identity (77.5%), superscription (83.74%), and inscription (78.98%). As a result, with more than half error in a prescription written in subscription and signature item, the failure of giving adequate therapy will cause a low recovery or healing process to the patients. Moreover, it may harm or cause death to the patients. In conclusion, more than half of medical students made common errors in prescription's writing.

Key words: Clerkship, error, prescription

# Kesalahan Penulisan Resep pada Mahasiswa Koasistensi Fakultas Kedokteran

#### Abstrak

Resep merupakan instruksi yang ditulis oleh tenaga medis untuk memberikan obat atau seperangkat alat kepada pasien. Peresepan yang tepat akan membawa proses pemulihan dan penyembuhan terhadap pasien. Mahasiswa kedokteran yang menjalankan masa koasisten harus memiliki kompetensi yang baik untuk memilih dan menuliskan terapi yang sesuai. Penelitian ini bertujuan menganalisis kesalahan umum dalam penulisan resep pada mahasiswa kedokteran yang akan menghadapi ujian akhir untuk menjadi seorang dokter. Penelitian ini menggunakan metode analitik terhadap 609 lembar resep dari 180 mahasiswa kedokteran yang sedang melaksanakan *try out* akhir *objective structured clinical examination* (OSCE) di Fakultas Kedokteran Universitas Islam Bandung pada Maret 2018. Dianalisis setiap komponen yang harus ada dalam penulisan resep, yaitu identitas pasien, superskripsi, inskripsi, subskripsi, dan *signature*. Hasil penelitian menunjukkan bahwa lebih dari setengah mahasiswa melakukan kesalahan pada item subskripsi (50,25%) dan *signature* (55,83%), sedangkan sebagian besar sudah menulis dengan baik pada item identitas pasien (77,5%), superskripsi (83,74%), dan inskripsi (78,98%). Akibatnya, dengan lebih dari setengah jumlah kesalahan dalam penulisan item subskripsi dan *signature* maka kegagalan dalam memberikan terapi yang adekuat dapat menyebabkan angka kesembuhan yang rendah, terlebih lagi dapat menimbulkan bahaya bahkan kematian terhadap pasien. Simpulan, lebih dari setengah mahasiswa kedokteran melakukan kesalahan umum dalam penulisan resep.

Kata kunci: Kesalahan, koasisten, resep

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## Introduction

The Institute of Medicine estimated that more than 1 million preventable adverse events occur each year in the United States. That report also estimated that, in the United States, up to 98,000 annual deaths can be attributed to medical errors, with errors and preventable deaths costing \$30 billion annually in lost income and excess health care expenditures. Historically, errors in medicine were thought to be an unavoidable outcome of learning to practice medicine.<sup>1</sup>

Today, most experts agree that a majority of medical errors are attributable to faulty systems, processes, and conditions rather than the failure of individuals. However, some argue that at the same time we emphasize the way systems can lead to errors, it also is essential to create an environment in which medical students and house officers can discuss and learn from individual mistakes, and learn how to report and respond to such mistakes.<sup>2</sup>

Drug-related problems are one of the most common reasons for hospitalization, and most of these problems are considered to be avoidable. In turn, a significant proportion of drug-related problems are due to prescription errors. Frequent mistakes relate to over-medication, undermedication, the prescription of non-indicated drugs, wrong doses, or ambiguous dosage ordering.<sup>3</sup>

The prescription is an instruction written by a medical practitioner to give a drug or device for a patient. Prescription writing is one of the most critical activities in the health care system of every country. Most of the physicians demonstrate their skills by writing a prescription, which considered as the first step of medical intervention.<sup>4,5</sup>

The prescription writing is a complex and challenging skill which depends on the physician's diagnostic skills, comprehensive pharmacological knowledge, communication skills, understanding of the principles of clinical pharmacology, the ability to make decisions regarding the potential risks vs benefits, and clinical experiences. The proper prescription will support recovery or healing process for the patient. Medication errors in hospitals have been reported to occur with alarming frequency with the vast majority involving junior doctors recently graduating from medical school.<sup>4,5</sup>

The prescribing errors have classified into different categories based on knowledge, rules, action, and memory. The knowledge-based errors reflect a lack of experience or understanding of specific medications. Rule-based errors reflect the lack of application of the fundamental rules. Action-based errors are those not intended (e.g., misspelling or mistaken drug name). Memory-based errors involve forgotten information (e.g., patient allergy).<sup>6</sup>

Clerkship students must have an excellent competency to choose the right medication and write down an appropriate drug or therapy. Recently graduated doctors are known to be most prone to committing prescription errors. Medical students are generally expected to acquire their prescribing skills during clerkships.<sup>2</sup> Interestingly, there are currently no data available regarding the validity of this assumption. Therefore, in this study, we refer to analyze a standard error in prescription's writing in clerkship students at their final examination to be a medical doctor.

#### Methods

Every medical student requires to complete clinical clerkships during their education before the national final examination. Students completed the clinical clerkships periods in the teaching hospitals. The theory supporting this type of design is that when participants are asked to respond clinical cases about how much they know about a particular subject after they have some basic knowledge of the subject itself, they are better able to accurately give accurate diagnosis and therapy based on their knowledge during the clinical clerkship's periods.

During the test, students were required to complete a patient's management based on the case include prescribing within a timeframe of 10 minutes per case. Study participation was voluntary, and the local ethics committee approved the study protocol.

We used the analytic method to 609 sheets of prescription from 180 clerkship students in their last try out the objective structured clinical examination (OSCE) at the Faculty of Medicine Universitas Islam Bandung in March 2018. We analyze the component that every prescription should have, which consists of patient identity (name, age, gender and occupation), superscription (writing R/symbol which means "take"), inscription (drug or medication prescribed), subscription (direction to pharmacist) and signature (direction how to use drug for the patient).

The statistical package of social sciences (SPSS/ PC) version 17 used for data entry and analysis. Calculations based on the table of proportions evaluation. We compared the averages of each group using this statistical analysis.

This study started after obtaining ethics approval from the Health Research Ethics Committee of Faculty of Medicine, Universitas Islam Bandung.

#### Results

Based on the Table, it could be concluded that most candidates wrote complete identities (77.5%), superscriptions (83.74%), and inscriptions (78.98%). Nearly half of clerkship students made an error in subscription (50.25%) and signature items (55.83%). Incompleteness dominates in terms of writing signature and subscription.

#### Discussion

Medication errors may have devastating, farreaching consequences, not limited solely to patients and their families. Many medication errors result from prescribing errors, which have an increased potential for serious complications. Prescribing errors have classified into different categories based on knowledge, rules, action, and memory.<sup>6</sup>

Table Proportion of Prescription Writing Completeness

Terms	n=609	Percentage
Patient identity		
Not complete	137	22.50
Complete	472	77.50
Superscription		
Not complete	99	16.26
Complete	510	83.74
Inscription		
Not complete	128	21.02
Complete	481	78.98
Subscription		
Not complete	306	50.25
Complete	303	49.75
Signature		
Not complete	340	55.83
Complete	269	44.17

One study found that most prescribing errors attributed to (1) lack of information about the patient; (2) specific drug therapy (e.g., narrow therapeutic index medications); or (3) inability to incorporate patient-specific factors (e.g., declining renal function) to appropriate selection and dosing of drug therapy. Other errors result from miscalculations, improper use of decimal points, unit or rate expressions, and nomenclature.<sup>6</sup>

Medication errors cause many adverse drug events (ADEs). Many of these medication errors are due to errors in prescription writing, like illegibility, ambiguous abbreviations, lack of date of prescription, dose, route, frequency of administration, and duration of treatment. Prescription writing and audit s taught to students as a part of the curriculum.<sup>6</sup>

Clerkships constitute an integral part of medical education, although it is not sufficient to rely on students systematically practicing skills as intended. Given the pivotal importance of patient safety for good clinical practice, correct prescribing represents a critical skill that trained at medical schools.<sup>2</sup>

Several studies have shown that structured problem-based training improves medical student's ability to prescribe correctly. Problem-based training with a focus on common prescription errors can reduce average error rates by more than 50%, independently of the clinical context. The students need to clear a practical examination conducted by the university that includes prescription writing.<sup>2,6</sup>

There are a general perception and concern that most medical schools neither provide adequate training opportunities nor carry out a robust assessment of students in drug prescribing skill. As a consequence of these curricular issues, new doctors are underprepared to take on prescribing responsibilities after graduation. Various models of teaching/learning clinical pharmacology and therapeutics proposed.<sup>7</sup>

Every prescription is a legal document, in which considering all medication characteristics is necessary; therefore, the error-free spelling of the full name of drugs, legibility, dosage form, strength, quantity, and proper instructions are of high significance. A typical drug prescription has standard components which fall into three categories: patient-related (name, age, and gender), physician-related (the identity of the prescriber) and drug-related (drug

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name, dose, formulation, route and frequency of administration, quantity to be dispensed, duration of treatment and directions for use).<sup>5,7,8</sup>

From the research result, nearly half of clerkship students made an error in subscription (50.25%) and the signature items (55.83%). Incompleteness dominates in terms of writing signature and subscription. Studies have shown that in about half of hospital admissions, physicians may make one prescribing error or the other. Errors are more likely to occur with junior doctors but are still prevalent in other senior categories of doctors. Errors in prescribing attributed to a variety of factors including individual, environmental, and organizational such as lack of knowledge, insufficient training, workload, and communication. Some researchers have reported that foundation (intern) year doctors lack confidence in prescribing several groups of medicines with the majority of them feeling that undergraduate education in clinical pharmacology and therapeutics had not prepared them adequately for prescribing duties.9

An error occurring at prescriptions writing stage may fail the therapy or may cause harm to the patient. Medication errors are recognized to be a significant impediment in providing optimum medical care to the patients. These errors harm patient's health and therefore should minimize.<sup>5–7</sup> Medication errors can give rise to adverse events too. In one study, 11% of adverse events were due to medication errors.<sup>10</sup>

Conventionally, all newly graduated clerkship students are required to undergo internship in accredited hospitals for a year before full registration to practice after they passed the national final board examination. The internship is a period of medical apprenticeship under the supervision of a consultant. The intern is expected to learn clinical skills, perform some clinical procedures, and demonstrate sound clinical judgment to arrive at patient management decisions. Junior doctors are the most frequent prescribers in the hospital setting and are reported to make most of the prescribing errors. Knowing what drug to prescribe to which the patient does not necessarily translate to proper prescription. Because junior doctors make the majority of prescription-related errors in the hospital environment, it is necessary to educate the clerkship student before internship periods and develop interventions that will improve the prescribing qualities. The broad aims of medical school training are to lay the foundation for a medical career and to provide junior doctors with appropriate knowledge and skills for the first stage of their post-qualification career.<sup>9</sup>

The Faculty of Medicine Universitas Islam Bandung introduced patient safety teaching into the preclinical curriculum. The curriculum of this institution has developed included problem identification, needs assessment, development of goals and objectives, choosing educational strategies, implementation, evaluation, and feedback. The institution sought an experiential learning environment to ground its curriculum in problem-based learning.

Our findings may help to explain how much clerkships student error in prescription writing in subscription and signature item. With more than half error in prescription writing in subscription and signature item, the failure of giving adequate therapy will cause a low recovery or healing process to the patients, moreover, it may harm or cause death to the patients.<sup>2</sup>

From Ajemigbitse et al.9 study, factors that could contribute to the possibility of prescribing errors occurring in the practice environment were; respondents considered workload (23, 76.7%), multitasking (19, 63.3%), rushing (18, 60%) and tiredness or stress (16, 53.3%) as important contributory factors. Other factors mentioned were a distraction (11, 36.7%), low morale (9, 30%), unfamiliar patient, busyness and no senior support (8, 26.7%) each, being nervous or confused (5, 16.7%) and time in the day (2, 6.7%). In this study setting, the error of prescription writing maybe has caused by timelimited and personal stress of final examination setting. The stress and performance anxiety involved with summative examinations could adversely affect decision-making abilities and the student's ability to writing the prescriptions effectively.5

Ideally, when clinical cases occur in the hospital, clerkship students would see appropriate responses and accurate prescription to handle the case by more senior clinicians. Observing senior physicians is a significant way in which medical students and young physicians learn appropriate behaviors. Clinical clerkship students can not only learn about the scientific and medical issues surrounding the safety error but also learn about the appropriate way to disclose and write an accurate prescription to the patients.<sup>2,11</sup>

Seiden et al.<sup>12</sup> suggest that training medical

students about the prevention and reporting of errors can help ensure patient safety. After analyzing a series of case studies in which medical students helped avert errors, they argue that since medical students have sufficient knowledge to recognize most error types and are responsible for the care of fewer patients, they can give more considerable attention to the details of clinical care and are a valuable, but untapped, resource for improving patient safety.<sup>2</sup>

Clerkship students need to practice these skills for themselves. Concerning patient safety and ensuring proper clinical practice among young doctors, specific training modules for writing good and a complete prescription within medical education would seem required on medical education universities. Medical teaching institution needs to develop an innovative and experiential curriculum that can be successfully delivered the medical students during a clinical clerkship and results changes in student ability to prescribe after they pass the final examination and become a doctor.

With more than half error in prescription writting in subscription and signature item, the failure of giving adequate therapy will cause a low recovery or healing process to the patients. Moreover, it may harm or cause death to the patients.

This study assessed the prescriptions-error of clerkship students. Results will be added to other evidence to serve as part of a needs assessment for future training. The authors intend to create and offer a prescription-error educational session explicitly designed for clerkship students. However, further research is needed to determine the most appropriate teaching methods to increase prescribing ability. Future studies not only will serve to enhance professional education, but also optimize patient medication safety.

It is essential to critically examine the level of prescribing competence expected from students at different stages of the program. We need to examine what should be the prescribing skill performance standard in preclerkship phase, clerkship phase, and final examination phase for medical students as outcomes.

# Conclusion

As a conclusion of this study was more than half of the clinical clerkship among medical students at their final examination to be a medical doctor made common errors in prescription's writing.

#### **Conflict of Interest**

There is no conflict of interests.

# Acknowledgement

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# **RESEARCH ARTICLE**

# Effects of Metformin, Avocado Seed, and Diabetic Ingredients Infusion to Weight and Fasting Blood Glucose on Sucrose Diet Rats

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#### Abstract

Metformin, an oral hypoglycemic drug which has metabolic effects and weight loss after 6-9 months; however, after 18 months, these effects disappear. Oral hypoglycemic drugs with no effect on raising the weight are needed. The objective of the study is comparing the effects of metformin, avocado seed infusion (AS), and diabetic ingredients/ DI (green chiretta, Java tea, and bitter grapes) in increasing weight and fasting blood glucose of rats with sucrose diet. The research was conduct at the Pharmacology Laboratory, Faculty of Medicine Universitas Kristen Maranatha in February–August 2017. The results showed that metformin within six weeks reduced weight (75.55%) compared to control (+) with a hypercaloric diet (114.36%). Metformin and hypercaloric diet in rats for 14 weeks showed a 125.66% increase in weight, higher than control (+) (114.36%), although not significant (p>0.05). Weight in rats with hypercaloric and AS diet for 14 weeks was 94.30% and 81.68% in DI was lower than control (+) (114.36%), but not significant (p>0.05). Fasting blood glucose (FBG) of dietary hypercaloric rats and metformin was 123.75 mg/dL, higher than control (+) (p>0.05). In conclusions, metformin increased rats body weight even though not significant to control (+) (p>0.05). In conclusions, metformin increased rats body weight even though not significantly and fasting blood glucose in rats fed a hypercaloric diet for 14 weeks, while avocado seed infusion and diabetic ingredients infusion did not.

Key words: Avocado seed, diabetic ingredient, fasting blood glucose, metformin, weight

# Efek Metformin, Infusi Biji Alpukat, dan Infusi Ramuan Diabetes terhadap Berat Badan dan Glukosa Darah Puasa pada Tikus Diet Sukrosa

#### Abstrak

Metformin, obat hipoglikemik oral berefek metabolik dan menurunkan berat badan (BB) setelah 6–9 bulan, namun setelah 18 bulan efek ini hilang. Diperlukan obat hipoglikemik oral yang tidak berefek meningkatkan BB. Tujuan penelitian ini membandingkan efek metformin, infusi biji alpukat (BA), dan infusi ramuan diabetes/RD (sambiloto, kumis kucing, dan bratawali) dalam meningkatkan BB dan glukosa darah puasa pada tikus diet sukrosa. Penelitian dilaksanakan di Laboratorium Farmakologi, Fakultas Kedokteran Universitas Kristen Maranatha periode Februari–Agustus 2017. Hasil penelitian menunjukkan metformin dalam waktu 6 minggu mengurangi penambahan BB (75,55%) dibanding dengan kontrol (+) diet hiperkalori (114,36%). Pemberian metformin dan diet hiperkalori pada tikus selama 14 minggu menunjukkan kenaikan BB 125,66%, lebih tinggi dibanding dengan kontrol (+) (114,36%), walaupun tidak signifikan (p>0,05). Berat badan pada tikus dengan diet hiperkalori dan infusi BA selama 14 minggu adalah 94,30% dan RD 81,68%, lebih rendah dibanding dengan kontrol (+) (114,36%), namun tidak signifikan (p>0,05). Glukosa darah puasa (GDP) tikus diet hiperkalori dan metformin adalah 123,75 mg/dL, lebih tinggi dibanding dengan kontrol (+) 85,75 mg/dL (p<0,01), sedangkan GDP infusi BA dan RD selama 14 minggu adalah 85,75 mg/dL dan 99,50 mg/dL, tidak signifikan terhadap GDP kontrol (+) (p>0,05). Simpulan, metformin meningkatkan berat badan tikus walau tidak signifikan dan meningkatkan glukosa darah puasa pada tikus diet hiperkalori (+) (p>0,05). Simpulan, metformin meningkatkan berat badan tikus walau tidak signifikan dan meningkatkan glukosa darah puasa pada tikus diet hiperkalori (+) (p>0,05). Simpulan, metformin meningkatkan berat badan tikus walau tidak signifikan dan meningkatkan glukosa darah puasa pada tikus diet hiperkalori selama 14 minggu, sedangkan infusi biji alpukat dan ramuan diabetes tidak.

Kata kunci: Berat badan, biji alpukat, gula darah puasa, metformin, ramuan diabetes

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# Introduction

Metformin is a widely used drug for type 2 diabetes mellitus treatment. The hypoglycemic effect of metformin caused by decreasing production of liver glucose and increasing usage of glucose. Metformin has a beneficial effect on fat that can reduce fatty liver. AMP-activated protein kinase (AMPK) is the primary regulator at the cellular level for fat and glucose metabolism. Metformin activates AMPK that decrease the activity of acetyl-CoA carboxylase (ACC) in hepatocytes, induce fatty acid oxidation, and suppress the expression of the lipogenic enzyme. Thus, the effect of metformin on inhibiting glucose production in the liver and increasing usage of glucose by muscle cell is through AMPK activation. AMPK is a multisubunit enzyme that regulates to biosynthesis fat by its role in phosphorylating and inactivate acetyl-CoA enzyme. AMPK has a full function in metabolism, such as metabolism of fatty acid, uptake glucose by muscle, and glucose-stimulated genes associated with liver lipogenesis, include fatty acid synthase (FAS). Chronic activation of AMPK may include muscle hexokinase expression, and glucose transporter, which has the mimicry effect of extensive physical exercise. AMPK activation has the right approach for handling type 2 DM. Metformin has metabolic effects through activation of AMPK.1 Metformin used in the treatment of type 2 diabetes mellitus and has an additional effect of reducing weight.<sup>2</sup>

The results of a meta-analysis of 11 studies published in 1995 about a patient that was given metformin or sulfonylurea 6-52 weeks, including nine studies that obtained information about changes in body weight.3 The use of sulfonylureas associated with increased body weight seen in all studies.<sup>3-5</sup> Weight loss in metformin was seen in 7 studies, increasing body weight in 2 studies.3 The metformin decreases body mass index (BMI) -1.38 (95% CI -1.93 to -0.82) kg/m<sup>2</sup> after six months, while the effect of giving metformin over 12 months of treatment the results were not significantly different compared to placebo. Weight loss with metformin achieved after 6-9 months; then after 18 months, the BMI returns to its BMI before treatment.6

The BMI correlates with the development of type 2 diabetes mellitus. Every 1 kg increase in excess weight has a risk of 49% for the development of type 2 diabetes mellitus within ten years.<sup>7</sup> Women of childbearing age who are obese have a risk of getting type 2 diabetes 2.63 times greater than women of childbearing age who are not obese.<sup>8</sup>

Therefore, research on blood glucoselowering agents that do not cause weight gain needs to be developed, especially for the treatment of diabetes mellitus. Traditionally, people treat diabetes mellitus with avocado seed. A study conducted an assessment of the antidiabetic activity of avocado seed extract (Persea americana Mill) with glucose tolerance test method, with the resulting decrease of concentration of glucose.<sup>9-12</sup> Also, the community also uses diabetic ingredients consisting of green chiretta (Andrographis paniculata (Burm. f.) Nees), Java tea (Orthosiphon stamineus Benth), and bitter grapes (Tinospora rumphii Boerl) to treat diabetes mellitus.<sup>13-18</sup> Both the avocado seeds and the diabetic ingredients (green chiretta, Java tea, and bitter grapes) are expected not to have the effect of increasing body weight when used as an oral hypoglycemic drug. This study was conducted to obtain oral hypoglycemic drugs that did not affect increasing body weight, and the aim was to compare the effects of metformin, avocado seed infusion (AS), and diabetic ingredients/ DI infusion (green chiretta, Java tea, and bitter grapes) on increasing body weight of rats with sucrose diet.

# Methods

The design of this study was an experimental laboratory study with experimental animals Wistar rats aged two months with a hypercaloric diet in the form of drinking water 20% sucrose (w/v). This research conducted at the Pharmacology Laboratory, Faculty of Medicine Universitas Kristen Maranatha in February–August 2017.

The treatment groups (n=4) are (1) Metformin A group, rats were given a hypercaloric diet for eight weeks, then hypercaloric diet & metformin for six weeks; (2) Metformin B group, rats were given a hypercaloric diet+metformin for 14 weeks; (3) Avocado seeds A group, rats were given a hypercaloric diet for eight weeks, then hypercaloric diet+AS infusion dose of 0.5 g/kgBW for six weeks; (4) Avocado seeds B group, rats were given a hypercaloric diet+AS infusion dose of 0.5 g/kgBW for 14 weeks; (5) Diabetes ingredients infusion A group, rats were given a hypercaloric diet+DI infusion (green chiretta, Java tea, and bitter grape = 1:1:2) dose of 0.5 g/kgBW for 6

weeks; (6) Diabetes ingredients infusion B group, rats consumed a hypercaloric diet+DI infusion (green chiretta, Java tea, and bitter grapes = 1:1:2) dose of 0.5 g/kgBW for 14 weeks; (7) Positive control, rats were given a hypercaloric diet for eight weeks and hypercaloric diet for six weeks; and (8) Negative control, rats were given pellets and distilled water without a hypercaloric diet for 14 weeks.

The measured data is the weight of each group that then was performed a statistical test with the one-way ANOVA and the Tukey HSD test with alpha=0.05.

This research approved by the Research Ethics Committee of the Faculty of Medicine Universitas Kristen Maranatha-RS Immanuel Bandung with letter number: 230b/KEP/VIII/2017.

#### Results

The study began with weighing the weight of experimental animals before treating. The results of rats body weight measurements before and after treatment has presented in Table 1.

#### Discussion

The results showed that experimental animals

of rats fed a hypercaloric diet with sucrose administration of 20% (w/v) in drinking water for 14 weeks showed an increase in body weight of 114.36%. Pre-experimental weight was 159.5 gram, and after 14 weeks of the hypercaloric diet, the weight of rat was 341 gram. Weight of the rat without hypercaloric diet was 157.75 gram, and after 14 weeks the rat weighed 295.75 gram, increase 87.80%. Weight of rat that were given a hypercaloric diet in 8 weeks and after that was given hypercaloric diet and metformin in 6 weeks was 157 gram and became 276.25 gram after 14 weeks, increase 75.55%. This result shows that metformin can reduce weight in 6 weeks compare to hypercaloric diet rats (114.36%) and negative control (87.80%). Giving metformin and a hypercaloric diet in rats for 14 weeks showed a weight gain of 125.66%, a pretreatment body weight of 162.5 grams to 363.75 grams after treatment. This result shows an increase of weight in rats that with metformin and hypercaloric diet in 14 weeks, the enhancement is higher (125.66%) compare to hypercaloric diet in 14 weeks only (114.36%), even though the difference is not significant (p>0.05).

Being overweight and obese increases the risk of cardiovascular disease, various types of cancer, and various other health problems.<sup>19</sup>

Courses a	Weight of Rats in Group (gram)							
Groups	MA	MB	AS-A	AS-B	DI-A	DI-B	K+	К-
Before treatment								
Rat 1	141	166	159	180	175	188	163	189
Rat 2	156	177	132	169	172	149	158	140
Rat 3	161	154	172	168	172	154	168	158
Rat 4	170	153	164	170	170	191	149	144
Mean	157	162.5	156.75	171.75	172.25	170.5	159.5	157.75
Treatment in 8 weeks								
Rat 1	186	261	277	195	282	260	278	276
Rat 2	260	291	220	252	281	327	275	218
Rat 3	194	206	236	297	283	301	268	251
Rat 4	335	279	270	233	244	237	282	241
Mean	243.75	259.25	250.75	244.25	272.5	281.25	275.75	246.5
Treatment in 14 weeks								
Rat 1	228	397	278	307	297	244	349	340
Rat 2	316	296	299	363	328	364	330	247
Rat 3	241	422	296	347	294	352	333	309
Rat 4	320	340	289	315	338	237	352	287
Mean	276.25	363.75	290.5	333	314.25	299.25	341	295.75

Table 1 Measurements of Rats Weight Before and After Treatment

The result of one-way ANOVA p≥0.05, MA: metformin A group, MB: metformin B group, AS-A: avocado's seed A group, AS-B: avocado's seed B group, DI-A: diabetes ingredients A group, DI-B: diabetes ingredients B group, K+: positive control, K−: negative control

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Dete		Percentage of Rats Weight Increase						
Rats	MA	MB	AS-A	AS-B	DI-A	DI-B	K+	К-
1	61.70	139.16	74.84	70.56	69.71	29.79	114.11	79.89
2	102.56	67.23	126.52	114.79	90.70	144.30	108.86	76.43
3	49.69	174.03	72.09	106.55	70.93	128.57	98.21	95.57
4	88.24	122.22	76.22	85.29	98.82	24.08	136.24	99.31
Mean	75.55	125.66	87.42	94.30	82.54	81.68	114.36	87.80

 Table 2 Percentage of Rats Weight Increase After 14 Weeks

The result of one-way ANOVA p≥0.05, MA: metformin A group, MB: metformin B group, AS-A: avocado's seed A group, AS-B: avocado's seed B group, DI-A: diabetes ingredients A group, DI-B: diabetes ingredients B group, K+: positive control, K−: negative control

Table 3 Fasting Blood Glucose Level in Rats After 14 Weeks Treatment

Rats	F	asting Blo	od Glucos	se Measur	ement in	Each Gro	up (mg/dI	L)
Kats	MA	MB	AS-A	AS-B	DI-A	DI-B	<b>K</b> +	К-
1	88	113	108	79	94	89	83	96
2	107	122	118	91	103	89	101	104
3	108	119	116	95	95	110	80	93
4	122	141	111	78	106	110	79	103
Mean	106.25	123.75	113.25	85.75	99.5	99.5	85.75	99

The result of one-way ANOVA p≥0.05, MA: metformin A group, MB: metformin B group, AS-A: avocado's seed A group, AS-B: avocado's seed B group, DI-A: diabetes ingredients A group, DI-B: diabetes ingredients B group, K+: positive control, K−: negative control

Table 4 Tukey HSD	Test Result of	f Fasting Bl	ood Glucose	Level in	Rats After 14	Weeks
Treatment						

	Fasting Blood Glucose Measurement (mg/dL)							
	MA 106.25	MB 123.75	AS-A 113.25	AS-B 85.75	DI-A 99.5	DI-B 99.5	K+ 85.75	K– 99
MA 106.25		NS	NS	NS	NS	NS	NS	NS
MB 123.75			NS	**	*	*	**	*
AS-A 113.25				*	NS	NS	*	NS
AS-B 85.75					NS	NS	NS	NS
DI-A 99.5						NS	NS	NS
DI-B 99.5							NS	NS
K+ 85.75								NS
K– 99								

NS: not significant, \*significant, \*\*very significant, MA: metformin A group, MB: metformin B group, AS-A: avocado's seed A group, AS-B: avocado's seed B group, DI-A: diabetes ingredients A group, DI-B: diabetes ingredients B group, K+: positive control, K-: negative control

Therefore, oral hypoglycemic agents that can reduce glucose and do not increase of weight need to be developing. Research that assesses the antidiabetic activity of avocado seed extract (*Persea americana* Mill), with glucose tolerance test method with the result of lowering blood glucose levels has conducted by Zuhrotun.<sup>19</sup> Phytochemical screening of simplicia and ethanol extract of avocado seeds showed polyphenols, tannins, flavonoids, triterpenoids, quinones, monoterpenoids, and sesquiterpenoids.

Also, the community used diabetic ingredient consisting of the green chiretta (Andrographis paniculata [Burm. f.] Nees), the Java tea (Orthosiphon stamineus Benth), and the bitter grape (Tinospora rumphii Boerl). The bitter grape has the main content: diterpene lactone, including andrographolide, and andropanoside. The green chiretta effect includes antipyretic, antimalarial, and anti-inflammatory. Java tea has the main content: glycoside orthophony, essential oil, saponin, saxophone, and potassium salt. The effects of Java tea include diuretics effect. The bitter grape has the main content: berberine alkaloids, columbine, picroretoside glycosides, and picroretin bitter substances. Bitter grape's stem has the effect of lowering blood glucose levels.<sup>17,18,20</sup> Both the avocado seeds and the diabetic ingredients that consist of green chiretta, Java tea, and bitter grape which have the potential as oral hypoglycemic drugs, should not have the effect of increasing body weight.

This study showed an increasing weight on rats that were given hypercaloric diet and avocado's seed in 14 weeks was 94.30%, lower than the positive control (114.36%), even though is not significantly different (p>0.05). The body weight of rats with a hypercaloric diet and diabetic ingredients infusion for 14 weeks showed an increasing rats weight 81.68%, lower than the increase in body weight of rats who received a hypercaloric diet only (114.36%), even though isn't significantly different (p>0.05).

The study also showed that average of fasting glucose levels in rats given metformin and a hypercaloric diet was 123.75 mg/dL, higher than fasting blood glucose levels in rats with a 14 weeks hypercaloric diet (85.75 mg/dL) with significantly different (p<0.01), with a mechanism that needs to be studied and examined further. Whereas, an average of fasting blood glucose levels of rats that received a hypercaloric diet and avocado seed infusion for 14 weeks was 85.75 mg/dL, an average of fasting blood glucose levels of

rats receiving a hypercaloric diet and diabetes ingredients infusion was 99.50 mg/dL. Both of these fasting glucose levels were not significantly different (p>0.05).

#### Conclusions

Metformin increased rats body weight even though not significantly and fasting blood glucose in rats fed a hypercaloric diet for 14 weeks, while avocado seed infusion and diabetic ingredients infusion did not increase rats body weight and fasting blood glucose compared to controls who received a 14 weeks hypercaloric diet.

# **Conflict of Interest**

The authors declare no conflict of interests.

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## **RESEARCH ARTICLE**

# **Reproductive Health Problems in Adolescents in Banten Province**

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#### Abstract

Teenagers are the next generation that needs to be the center of attention. Physical and mental development in adolescents occurs rapidly. The process of changing times with free association arises causing debate about their reproductive health. The purpose of this study was to determine the reproductive health problems of adolescents in Banten province. This study used a qualitative design and constructivism paradigm. The research method was using the in-depth interview guideline instrument with 11 informants conducted in Banten province in January–June 2017. Qualitative data analysis using content analysis. The results showed that environmental factors such as family, relationships, health workers, and the availability of prostitution practice were trigger teenagers' problems. The environment did not support them to learn about sexuality makes them seek information from sources that cannot be justified. This practice made adolescents have inappropriate knowledge about adolescent reproductive health. The availability of prostitution practice was a unique highlight for those who can channel their curiosity in fulfilling their sexual desires. In conclusions, adolescent reproductive health problems in Banten province consisted of premarital sex behavior, teenage pregnancy, teenage marriage, youth delivery, sexually transmitted diseases, and abnormal sexual behavior. These problems arise due to factors of knowledge, environment, and family economic status.

Key words: Adolescent, reproductive health, sexuality

# Permasalahan Kesehatan Reproduksi pada Remaja di Provinsi Banten

#### Abstrak

Remaja merupakan generasi penerus yang perlu menjadi pusat perhatian. Perkembangan fisik dan mental pada remaja terjadi secara pesat. Proses perubahan zaman dengan pergaulan bebas memicu timbulnya permasalahan kesehatan reproduksi pada mereka. Tujuan penelitian ini mengetahui permasalahan kesehatan reproduksi remaja di Provinsi Banten. Penelitian ini menggunakan desain kualitatif dan paradigma konstruktivisme. Metode penelitian menggunakan instrumen wawancara mendalam kepada 11 informan yang dilakukan di Provinsi Banten pada bulan Januari–Juni 2017. Analisis data kualitatif menggunakan analisis konten. Hasil penelitian menunjukkan bahwa faktor lingkungan seperti keluarga, pergaulan, tenaga kesehatan, dan ketersediaan tempat prostitusi memicu permasalahan remaja. Lingkungan yang tidak mendukung mereka untuk belajar tentang seksualitas membuat mereka mencari informasi dari sumber yang tidak dapat dipertanggungjawabkan kebenarannya. Hal tersebut membuat remaja memiliki pengetahuan yang tidak tepat tentang kesehatan reproduksi remaja. Ketersediaan tempat-tempat prostitusi menjadi sorotan khusus bagi mereka yang dapat menyalurkan keingintahuan mereka dalam memenuhi hasrat seksualitas. Simpulan, permasalahan kesehatan reproduksi remaja, penyakit seksual, dan perilaku seks menyimpang. Permasalahan tersebut muncul karena faktor lingkungan, pengetahuan, dan ekonomi keluarga.

Kata kunci: Kesehatan reproduksi, remaja, seksualitas

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# Introduction

Adolescence is a period of transition from childhood to adulthood. Teenagers will experience physical, cognitive, and social-emotional changes according to their age. During this time, the reproductive organs begin to function so that they require attention in their reproductive health.<sup>1</sup>

Based on the 2012 Indonesian Demographic and Health Survey (IDHS), premarital sex behavior in adolescents is quite high. This results based on an unhealthy dating style that can lead to premarital sex. Premarital sex occurs out of curiosity (57.5% of men), instinct (38% of women), and forced by a partner (12.6% of women). They reflect the lack of understanding of adolescents about the risk of sexual relations and the ability to reject relationships that they do not want.<sup>2-4</sup>

Condom use in adolescents is also the center of attention. The percentage of condom use in adolescents has increased from 18% in 2007 to 21.8% in 2012. Increasing condom use will increase the risk. The risks posed are unwanted pregnancies and sexually transmitted infections. This amount is a concern for the Banten region because 4.5% of the total teenage population is in Banten province.<sup>5</sup>

The problems faced by adolescents at this time can affect the number of maternal and child mortality. Out of wedlock sex problems are happen in adolescents that cause unwanted pregnancies and increase the number of child marriages (adolescents). These pregnancies can pose a risk of death because of abortion, complications of pregnancy, and childbirth. The risk of free sex can also cause sexually transmitted infections (STIs) or HIV/AIDS in adolescents.<sup>6</sup> The proportion of married age in adolescents based on sex shows that women are twice as big as men. In 2012, one in one hundred girls aged 15 years in Indonesia became a mother.<sup>5</sup>

Banten province is the fifth most important and most populous region in Indonesia. The population increase in Banten province mostly comes from migrant residents. This condition influenced because of north Banten (Tangerang area) is a hinterland area for the Special Capital Region of Jakarta. Banten province is also an industrial area that is supported by its strategic location in the distribution both by land, sea, and air. The existence of Merak port as an existing sea transportation route in the Sunda Strait and Soekarno Hatta International Airport.<sup>7</sup> The purpose of this study was to determine the problems in adolescents related to reproductive health in Banten province.

# Methods

This study used a qualitative design and conducted in Banten province in January-June 2017. The participant selected using a purposive sampling technique. Data retrieval was done by interview method directly (face to face) to the informant. Interviews were conducted using interview guideline instruments made by researchers. The data collecting instrument consists of 5 (five) questions. The instrument developed based on the theme during the in-depth interview.

The informants used in this study were 11 people who lived in Banten province. Informants came from users of peer counseling services (counselors and counselees), health workers (obstetricians or gynecological obstetricians, pediatricians, and midwives) who provided reproductive health services, psychologists who provided adolescent counseling services, the National Population and Family Planning Board (*Badan Kependudukan dan Keluarga Berencana Nasional*/BKKBN), the Health Office, and the Information and Counseling Center for Youth (*Pusat Informasi dan Konseling Remaja*/PIK R).

This research had obtained a feasibility permit from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Padjadjaran Bandung with an ethical approval letter number: 47/UN6.C1.3.2/KEPK/PN/2017.

#### Results

The strategic location of Banten province is close to the National Capital to be a concern to pay more attention to the development of adolescent health. Based on the in-depth interviews, the problems in adolescents related to reproductive health in Banten province are as follows.

The cases of premarital sex behavior are still high in Banten province. Based on data recorded in the Banten Province Prevention of AIDS Commission that 40% of premarital sex practices in commercial sex workers in Banten province are adolescents aged 16–20 years.<sup>8</sup> Many stated that contributors to cases of premarital sexual behavior were carried out by urban teenagers. Free adolescent association in urban areas is one of the main factors causing it. However, cases of premarital sexual behavior do not only occur in urban areas but also villages. Premarital sexual behavior will bring new problems for adolescents, namely the occurrence of pregnancy outside of marriage.

"....in a village that I live for sure every year at least five children (junior high school-high school age) are pregnant out of wedlock...." (R3)

A lack of knowledge influences the premarital sexual behavior in adolescents in the Banten province. Teenagers perceive that sexual relations will make the body healthy because the calories produced are higher than the traditional exercise. Sexual desire that channeled makes them happy. They also stated that sexual intercourse did not cause pregnancy.

"....even though it's like sex (sexual intercourse) the calories are so much better than exercise, fun, and not necessarily pregnant too... from the searching in the web." (R10)

The knowledge about sexuality is influenced by ignorance in seeking information sources that can be justified. They will ask friends who might not know and even search for themselves through the internet according to the current digitalization era. Teenagers quickly get information through the internet from various authors. However, not all authors who provide information on the internet are experts in their fields.

Another factor that causes problems in adolescents is the environment. The environment around adolescents does not support sexuality. The sexual education approved in the school environment. However, it has not supported by the family environment. The family environment is vital because parents usually get less critical information about sexuality education. Sexuality education in adolescents considers as taboo by parents. They believe talking about sexuality with teenagers is similar to teaching them to do unwanted things.<sup>9,10</sup>

# "....in Banten the old people protest when sexuality taught in school." (R10)

In Banten province, it is also easy to find places of prostitution. The prostitution place usually concealed as a place of lodging (hotel), the entertainment place (karaoke), eating place (restaurant), and massage parlor. Everyone can enter the areas which offer an affordable price. This environment makes it easier for teens to channel their curiosity to sexuality.

"....I know such places start from the lowest and most expensive price in this place. They are even giving snacks (the commercial sex workers)." (R3)

Teenage pregnancy is a pregnancy that occurs at the age of under 20 years, regardless of married or unmarried women.<sup>11</sup> The adolescent pregnancy in Banten province is still high. The high number of pregnancy cases that occur in adolescents in Banten province sometimes is wanted. However, some are not wanted. An unwanted pregnancy is a pregnancy that occurs outside of marriage or pregnancy in teenagers who marry young. They have no plans to arrange births.

"....there are many (girls) under 20 years got pregnant. Some are out of wedlock, and some are married but don't want to get pregnant yet." (R3)

Pregnancy in adolescents usually happened due to teenagers' lack of knowledge about the pregnancy process and how to prevent pregnancy. They assume that having a relationship is okay, and there will be no consequence of pregnancy. Teenagers also do not understand about puberty phases, the fertile period, and the dangers of pregnancy in adolescents.

"There is someone who does not know what the fertile period is. We think that if sexual intercourse did only once, there no risks for health." (R10)

Teenagers who do not want pregnancy who are sexually active have usually lack information about contraception. Contraceptive information has provided by health workers only to those who are married. Health workers still hesitate in introducing contraception in adolescents. The unwanted teenage pregnancy cases in the Banten province occur mostly because of the pregnancy outside marriage.

"....he said he couldn't use a condom. Can you get married because you are pregnant? I think because it's for teenagers I tell the simple explanation, not long like those who are married...."(R3) The teenage marriage occurs before the age of 18 years.<sup>12,13</sup> This case is still high in Banten province both in villages and in urban areas. The number of adolescent pregnancy in rural areas is 13% higher than in urban areas 6%. Marriage occurs, and because of that, many teenagers do not continue their education or drop out of school. One of the economic factors of the family influenced them not to continue school. They cannot get good jobs other than traders, laborers, or farmers. They have no choice but to marry. They assume that by getting married, there will help make a living.

# "High school dropout rates are high, so where are you going if you don't get married." (R3)

The Banten government always improves the quality of education by providing educational facilities and infrastructure. Access to education (schools) is added to accommodate school-age residents according to their education level. However, based on the Banten Province Regional Statistics Report 2016, school enrollment rates are still low in the age of 16–18 years.<sup>7</sup>

Teenage marriage also occurs because of something unwanted like pregnancy outside marriage. The high number of premarital sex cases will have an impact on one of them is adolescent marriage. This marriage will add to the burden on parents both psychologically and economically.

# "....still in school, but reportedly was married because of 2 months pregnant." (R4)

Adolescent labor is labor that occurs under the age of 20 years. Childbirth is a health problem without seeing pregnancies outside of marriage or marriage. One of these teen births occurs because the knowledge of adolescents about the dangers of giving birth at an early age is still lacking. Childbirth in Banten province is still high. Youth or young childbirth is at risk of bleeding. Bleeding cases account for death in the mother. The high rate of delivery is comparable to the high maternal mortality rate (MMR) in Banten province. The total maternal mortality in Banten province in 2016 recorded at 240 people.<sup>14</sup> One of the causes of death is one that is too young to give birth.

"Many are still 15 years have children, 16 years have children, 19 years have children. I don't know what the complications are, and then the

# parents complain about me in trouble." (R1)

Adolescent childbirth indirectly has an impact on their parents. Teenagers still enjoy playing with their friends, and many of their children neglected, so their parents will become caregivers and meet their economic needs. The children become a burden on the adolescent parents.

The significant problem of sexually transmitted diseases such as sexually transmitted infections (STIs) and HIV/AIDS is also a problem that exists in adolescents in Banten province. One of these problems arises because of the consequences of premarital sex. Teenagers do not understand the signs and symptoms of sexually transmitted diseases. They consider the symptoms of STIs as a form of food poisoning.

# "....STIs he said it was sore throat...." (R3)

Information on sexually transmitted diseases (STDs) is already conducted regularly in Banten province. The Health Office and the BKKBN share information through the young health program (*pelayanan kesehatan peduli remaja*/PKPR) and PIK R. However, there are still teenagers who come to health services with STDs who do not understand the methods of transmission and prevention on them.

# "....teenagers are coming to the hospital... already with HIV." (R5)

Abnormal sexual behavior is also a problem for teenagers found in Banten province, for example, homosexuality.<sup>15</sup> Homosexuality is a personal, emotional, and sexual attraction to people of the same sex.

"....men like men, there are also fellow women... He does have experiences." (R11)

# Discussion

Based on the results of the study it was found that adolescent reproductive health problems in Banten province included premarital sexual behavior, teenage pregnancy, teenage marriage, youth delivery, sexually transmitted diseases (STIs and HIV/AIDS), and abnormal sexual behavior. These problems exist because they influence each other. The issue of adolescence did not only in urban areas but also in villages.

The problems of adolescents in Banten has

influenced by the knowledge factor. The result has following the results of Iswarati's<sup>16</sup> research that stated the knowledge of adolescents about the fertile period in Banten province was very low at 8.4%. They did not understand that unprotected sexual relations would lead to pregnancy and the risk of sexually transmitted diseases (STIs and HIV/AIDS).

Adolescents had unprotected premarital sexual intercourse without considering the impact or the risk so that an unwanted pregnancy occurs. A pregnancy that occurs can continue to unsafe abortion. Pregnancy at a young age has the chance of anemia, hypertension, eclampsia, premature birth, low birth weight (LBW), infection, and labor bleeding that can increase maternal and infant mortality.<sup>3,17,18</sup> In young mothers who gave birth, but were not ready physically and mentally and were supported by inadequate nutritional intake will cause intergenerational cycle of growth failure.<sup>3,17</sup>

Teenagers would prefer to seek reproductive health information through digital media rather than going to health workers. The internet was a place that is considered capable of meeting their needs without any "bad labels" from other people, especially for those who are sexually active. However, they did not realize that the information obtained from the internet could not all be true. Rohmavanti et al.19 in their study revealed that the youth-friendly health services were not optimal resulted in dissatisfaction and mistrust of teenagers towards health workers. They were worried that the results of their medical examinations would be available for other people. The condition occurs due to a lack of proper communication to establish good relations between health workers and adolescents.

The environmental factors also influenced the problem of adolescents in Banten province. The family environment did not support their children to learn about sexuality in school. The family also did not teach teenagers about the importance of sexuality knowledge. The family environment was a significant hindrance in shaping adolescent behavior. The family closest to teenagers was parents. Teenagers who did not get sexual education from their parents, usually engage in risky sexual behavior earlier.<sup>20,21</sup>

The family factors also influenced child-age marriage in adolescents in the Banten province. Many parents agree to early marriage in hopes of achieving social and financial security for their children after marriage. Fadlyana and Larasaty's<sup>22</sup> research found that the reason for early marriage is often due to the fear of an extramarital pregnancy due to the promiscuity of teenagers.

The family economy also influenced marriage in adolescence. Some parents cannot afford to support their children to continue their education so that many teenagers drop out of school.13 The government has not reviewed the cost of school education to overcome this problem. The government was still trying to improve the quality of education by providing educational facilities and infrastructure.7 Those who do not continue their school did not have the opportunity to get good jobs. The jobs that they get is only low pay ones, which include farmers. laborers, traders, and household assistants. The type of employment encouraged them to marry young so that the family economy would be better. However, they did not think much about the impact of a young marriage for him and his family.

The age of adolescents was an age that is very concerned with relationships. They would be happier if they called "slang kids" so they could find as many friends as possible. However, the results of this study found that the social environment in adolescents could have a particular impact on them. Friends associating with lousy behavior will influence teens to follow it. Deviant behavior in question is smoking, alcoholic beverages, and drug abuse. This situation requires monitoring parents by creating quality relationships between children and parents. This relationship could help teens to choose friends with good behavior.<sup>23-25</sup>

Poor behavior from the environment would make the teenager misbehave. The problem had found in adolescents in Banten with the abnormal sexual behavior act because of bad experiences on sexual harassment. A study conducted by Fergusson et al.<sup>26</sup> in New Zealand states that sexual violence on children would harm their lives in the future. They can experience psychological, physical, and social health problems. Child sexual abuse would affect risky sexual practices in adolescents.<sup>27–29</sup>

The number of places of prostitution in Banten province made it easy to channel sexual desire. Risky sexual behavior (the use of prostitution) carried out by teenagers can be caused by his desire to channel intimacy desires, proof of selfesteem, and his tendency to experience. The adolescent problem behavior arises later on due to physical, sexual, or neglected childhood experiences.<sup>30,31</sup>

# Conclusions

Reproductive health problems in adolescents in Banten province consist of premarital sex behavior, teenage pregnancy, teenage marriage, youth delivery, sexually transmitted diseases, and abnormal sexual behavior. These problems arise due to factors of knowledge, environment, and family economic status.

# **Conflict of Interest**

The author states that there is no conflict of interest.

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# **RESEARCH ARTICLE**

# Primary Hippocampal Cell Culture and Its Application in Medical Researches

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#### Abstract

Studies in neuroscience can be performed in vitro and in vivo. In vivo studies will show significant results, but it is difficult to do and time-consuming. Primary hippocampal cell culture widely has used in neurobiological studies such as identifying the cellular mechanism of proteins, neuronal activity, and characteristics. The results of studies conducted on this cell culture will be very useful in discovering pathogenesis of a disease, the effect of a substance on the neuron, and neural basis of memory and learning. However, currently in Indonesia, primary hippocampal cell culture is still rare and difficult to do. The purpose of this study was to demonstrate that primary hippocampal cell culture can be done and developed in Indonesia and to review the application of it in medical researches. The study was an experimental study by obtaining neurons from animal's hippocampus was conducted in 2015–2018 at Department of Cell Biology, Graduate School of Medicine Osaka University and Faculty of Medicine Universitas Padjadjaran. The experimental animal was mice embryo gathered 17.5-days postcoitus. Enzymatic and mechanical methods collected primary hippocampal cells. The cells counted and cultured, which later were observed to see neuron differentiation. The average number of culture cells from 3 embryonic's hippocampus were 2.39×10<sup>6</sup>. Neuron differentiation observed on the first day and more visible and numerous on the third day after plating. In conclusion, primary hippocampal cell culture using hippocampus from one hemisphere of embryonic mice brain showed a sufficient number of cells to carry out research and showed neuron differentiation.

Key words: Hippocampus, neuron, primary cell culture

# Kultur Sel Primer Hipokampus dan Penggunaannya dalam Riset Kedokteran

#### Abstrak

Penelitian dalam neurobiologi dapat dilakukan secara in vitro dan in vivo. Penelitian secara in vivo sangat berdampak hasilnya, namun sulit dan memakan waktu yang lama. Kultur sel primer hipokampus banyak digunakan dalam penelitian neurobiologi seperti melihat mekanisme protein seluler, serta aktivitas dan karakteristik neuron. Hasil penelitian yang dilakukan pada kultur sel ini akan sangat bermanfaat dalam menemukan proses suatu penyakit, efek suatu zat terhadap sel saraf, dan kemampuan belajar serta memori. Akan tetapi, saat ini di Indonesia kultur sel primer hipokampus masih jarang dan sulit dilakukan. Tujuan penelitian ini adalah menunjukkan bahwa kultur sel hipokampus primer dapat dilakukan dan dikembangkan di Indonesia, serta meninjau penerapannya dalam riset kedokteran. Penelitian ini merupakan studi eksperimental dengan mengoleksi neuron dari hipokampus hewan coba yang dilakukan pada tahun 2015–2018 di Department of Cell Biology, Graduate School of Medicine Osaka University dan Fakultas Kedokteran Universitas Padjadjaran. Hewan coba berupa embrio mencit hari ke-17,5 pascakoitus. Sel primer hipokampus dikoleksi untuk dihitung dan dikultur menggunakan metode enzimatik dan mekanik. Observasi neuron pada kultur dilanjutkan dengan mengamati diferensiasi neuron. Rerata jumlah sel kultur dari 3 hipokampus adalah 2,39×10<sup>6</sup>. Diferensiasi neuron sudah tampak pada hari pertama dan makin jelas serta tampak pada hari ketiga pascapenanaman. Simpulan, kultur sel primer hipokampus menggunakan hipokampus dari salah satu sisi hemisfer otak menunjukkan jumlah sel yang cukup untuk melakukan suatu penelitian dan menunjukkan diferensiasi dari neuron.

Kata kunci: Hipokampus, kultur sel primer, neuron

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# Introduction

Neuroscience is a branch of science that studies about neurology, psychology, and biology. Neuroscience also develops along with other branches of science such as anatomy, physiology, biochemistry, and pharmacology of the brain and nerves.<sup>1</sup> The study in these fields can be performed in vitro and in vivo. In vivo studies can be done, but it is difficult and complicated. In vitro studies using neuron is very useful for observing the function, mechanism, and structure of the neuron. There are several ways to culture neuron, for example, by using cell lines or primary cell culture.<sup>2,3</sup>

Currently, cell lines are instrumental in neuronal cultures because cell lines are easy to culture, generate numerous cells that immortal, and homogenous. There are several cell lines currently in use, such as human SH-SY5Y cell lines. These cells have derived from the parental metastatic bone tumor cell line SK-N-SH by the subcloning cell. These cells have a similar characteristic with neuroblast.2,4 A human neuronally committed teratocarcinoma cell line called NT2 cell or Ntera can be used in neuronal cultures by treatment with retinoic acid or inhibitor of mitosis.2,5 Rat cell lines that derived from a pheochromocytoma of adrenal medulla called PC12.2,6 Although cell lines have various advantages, these cells have a significant disadvantage because the cells have a different physiological characteristic with the neuron in vivo. The differences can lead to a different result of the study.2,7

Primary cell culture does not come from the tumor cell, and the structure is similar to neuron in vivo.<sup>2</sup> There are several primary cell culture; one of them is primary hippocampal cell. The primary hippocampal cell obtained by culturing neuron from the hippocampus. Through this cell, learn about cell structure, function protein in the neuron, the pathogenesis of the disease, the effect of the drug on neuron and theories about memory and learning.<sup>8-12</sup> Currently, in Indonesia, primary hippocampal cell culture is rarely done because of a complicated and immortal cell. However, the primary hippocampal cell has an advantage compared to the cell lines such as the characteristic of primary hippocampal cell resemble nerve cell in vivo.2 The purpose of this study was to demonstrate that primary hippocampal cell culture can be done and developed in Indonesia and to review the application of it in medical researches.

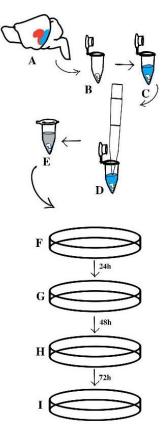
# Methods

This study design was an experimental study by obtaining neuron from mice embryos was conducted in 2015-2018 at the Department of Cell Biology, Graduate School of Medicine, Osaka University, Japan and Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia. Animals were treated according to the guidelines of the Animal Experimentation Committee of Osaka University (approval number: 21-045-0).13 Animals have given 12:12-h light-dark cycle with controlled humidity and temperature and free access to food and water. In this study, one male mouse and three female mice prepared. They prepared to copulating process. In the morning, a vaginal plaque was observed from the female mice to confirm mating process had occurred. Female mice that have vaginal plaque was separated and recorded as pregnant on the first day.14 After 17.5 days, the female mice sacrificed by cervical dislocation.15

Primary hippocampal cell culture performed according to the previous journal.<sup>11</sup> In brief, the embryo counted, and the brain collected from each embryo. The hippocampus separated from the brain. They were transferred to 1 mL of phosphate-buffered saline (PBS) containing 1% bovine serum albumin (BSA), deoxyribonuclease (DNase), papain, and glucose in 15 mL Falcon tube and put it again on the ice. The Falcon tube was incubated in a water bath at 37°C for 20 minutes. Using Pasteur pipette, the solution was triturated five times and incubated in the water bath at 37°C for 15 minutes. Pipetting five times again, and wait for several times. All supernatant aspirated without aspirated the pellet. After centrifugation, they plated on 35-mm dish pretreated with poly-D-lysine and laminin. They were cultured in neurobasal medium supplemented with B27 and GlutaMAX at 37°C in humidified 5% CO<sub>2</sub>.<sup>11</sup>

The cells were counted using hemocytometer under a microscope. They spread into the 35 mm dish, which already coated with poly-D-lysine, laminin, and neurobasal medium+10% fetal calf serum at 37°C and 5% humidity.

The cultured cells were observed under a stereotype microscope with a  $20 \times$  magnification objective lens at 24, 48, and 72 hours after plating. The morphology of the cell was rated by



#### Figure 1 Culture Procedure

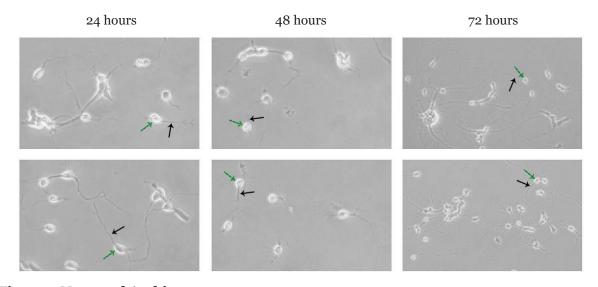
The schematic draw of the procedure. Hippocampal was collected from the fetal brain and proceed with the enzymatic procedures (A-E). Neurons were plated and observe sequentially (F-I) Table Number of Primary Hippocampal<br/>CellsNumber of<br/>HippocampusNumber of<br/>Cell (Cell/mL)Mean±SD12.35×1062.39×106)±<br/>(3.02×105)32.11×106(2.39×106)±<br/>(3.02×105)

measuring the neurite. Neurite was considered as axon if the length of the neurite was at least twice as long as any other process and was more than twice the diameter of the cell body.<sup>11,16</sup>

# Results

The primary hippocampal cell that had been cultured were counted using hemocytometer under a microscope. The results presented in Table. The mean number of cells from 3 hippocampi were  $2.39 \times 10^6$  cell/mL.

Primary hippocampal cell observation was done by looking neuron morphology at first until the third day (Figure 2). Neuron differentiation observed on the first day as an elongation of neurite from the cell body. Neurite considered as axon or dendrite according to its length. Differentiation was more visible and numerous



#### Figure 2 Neuronal Architecture

Micrographs of cultured hippocampal neurons at 24, 48, and 72 hours after plating to show neuron differentiation. Green arrow: cell body, black arrow: neurite

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on the 72 hours after plating.

## Discussion

Primary hippocampal cell culture is one of several methods to conduct a study in neuron.<sup>2,3</sup> Currently, in Indonesia, optimization of primary hippocampal cell culture is rare and challenging to do. The benefits of this culture are prodigious.<sup>2</sup> The cultured cells can use for study in many fields such as anatomy, physiology, biochemistry, pharmacology, and study about memory and learning.<sup>2,3,8-16</sup> By isolating and developing neuron from this culture, cell to cell interaction, cell structure, and protein in neuron observed.<sup>2,3</sup> Although the cells derived from this culture are not immortal and limited; they are similar to neuron in vivo. The results of the study come from using these cells are more significant.

From our study, the mean number of primary hippocampal cell culture was 2.39×10<sup>6</sup> cells/ mL. The cell observation under the microscope showed neuronal differentiation, especially after 72 hours after plating on the dish. Therefore, these results indicate that even though primary hippocampal cell culture is difficult, it is possible to do in Indonesia.

The applications of primary hippocampal cell culture in medical practices are numerous. Primary hippocampal cell culture could be used to discover the mechanism of a disease such as Alzheimer's disease. Hippocampal cell culture was used to discover the presence of extracellular fibrillar A $\beta$  in amyloid plaque, and intraneuronal neurofibrillary tangles consist of aggregated hyperphosphorylated tau, and elevated brain levels of soluble amyloid-beta derived diffusible ligands (ADDLs).9 The study found that in Alzheimer's disease, tau phosphorylation cultures of hippocampal neurons stimulated by ADDLs. Other studies using primary hippocampal cell culture showed that tau had a dendritic function. Tau-targeted NMDA receptor in postsynaptic, it has direct implications for pathogenesis and treatment of Alzheimer's disease.<sup>17</sup>

Primary hippocampal cell culture is also used to discover the role and mechanism of protein in the neuron. One study with primary hippocampal cell culture discovered that the role of vesicleassociated membrane protein 7 (VAMP7) or tetanus insensitive vesicle-associated membrane protein (TI-VAMP) on the neuronal outgrowth. The study used primary hippocampal cells from VAMP7 knockout (KO) mice and discovered that axonal elongation in KO mice was impaired. The study did not find the degradation of neuron-glia cell adhesion molecule (NgCAM) by immunofluorescence micrograph.<sup>10</sup> Other study using this culture, discovered that depletion of PKD1 and PKD2 affects axonal elongation. This study showed the role of PKD1 and PKD2 in axonal elongation.<sup>11</sup>

Primary hippocampal cell culture was used to discover the protective effect of salidroside for neuron. Salidroside has taken from Rhodia rosea. This study showed salidroside had protection effect to  $H_2O_2$  by reducing the activity of caspase-3, production of nitrite oxide (NO) and NO synthase. This effect can be used to develop salidroside as an agent to prevent or treat the neuronal injury in neurodegenerative disease.12 Besides, other studies of peptides that have a function similar to brain-derived neurotrophic factor (BDNF) were also conducted to test therapeutic effects in disorders with BDNF levels. It found that BDNF peptides were nontoxic to nerve cells in vitro in the hippocampal primary culture. Also, B-3 peptide that is one of the five tetrapeptides tested has a potential neuroprotective effect on the toxicity of H<sub>2</sub>O<sub>2</sub>.<sup>18</sup>

# Conclusions

Primary hippocampal cell culture using hippocampus from one hemisphere of embryonic mice brain showed a sufficient number of cells to carry out research and showed neuron differentiation. This study also demonstrates that primary hippocampal cell culture can be done and developed in Indonesia.

# **Conflict of Interest**

The authors declare no conflict of interests.

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# **RESEARCH ARTICLE**

# Soyghurt Supernatant on Mouse Embryonic Fibroblast (MEF) Cell

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#### Abstract

Yogurt is a functional food developed with various modifications in the fermentation process. Replacing animal milk into soymilk as raw material is one approach. Yogurt has a good effect on human health. Probiotic and bioactive compounds in vogurt can inhibit cell proliferation and stimulate apoptosis on the cancer cell line. However, there is no report about the effect of yogurt on a normal cell. This research was conducted to examine the impact of soyghurt supernatant intervention toward the viability of mouse embryonic fibroblast (MEF) cell. The is an in vitro study using MEF cell isolated from 10th days gestational age mice embryo conducted at Microbiology Laboratorium and Cell Culture and Cytogenetic Laboratory, Universitas Padjadjaran, Bandung in November 2018-January 2019. Sovghurt made from sovmilk fermented by Lactobacillus bulgaricus ATCC 11842. The number of the bacterial colony calculated by total plate count (TPC) method and pH calculated by pH meter. Soyghurt supernatant was made from soyghurt and then intervened into MEF cells by 1-20% concentration. The cell viability showed in the 50% inhibitory concentration (IC<sub>50</sub>) analysis. The intervention of soyghurt supernatant at 1–20% concentration showed there was no proliferation inhibition until 50% population ( $IC_{50}$ ). However, from the morphology analysis, there was MEF cell morphology alteration on the group given soyghurt supernatant with >12.5% concentration. Counter mechanism effect from soymilk fermentation by probiotic could be the driver for this result. In conclusion, soyghurt supernatant intervention at 1-20% concentration did not have a cytotoxic effect on MEF cell, but enhancement of soyghurt supernatant concentration can increase cytotoxic potential.

Key words: Cell viability, MEF cell, soyghurt supernatant

# Supernatan Soyghurt pada Sel Mouse Embryonic Fibroblast (MEF)

#### Abstrak

Yoghurt merupakan functional food yang dikembangkan dengan berbagai modifikasi dalam proses pembuatannya. Mengganti susu hewan dengan susu kedelai sebagai bahan baku adalah salah satunya. Yoghurt memiliki efek yang baik bagi kesehatan manusia. Senyawa probiotik dan bioaktif pada yoghurt dapat menginhibisi proliferasi sel dan menstimulasi apoptosis pada sel lini kanker. Akan tetapi, tidak terdapat laporan mengenai efek yoghurt pada sel normal. Penelitian ini dilakukan untuk menguji pengaruh intervensi supernatan soyghurt terhadap viabilitas sel mouse embryonic fibroblast (MEF). Ini adalah penelitian in vitro menggunakan sel MEF yang diisolasi dari embrio tikus hari ke-10 usia kebuntingan yang dilakukan di Laboratorium Mikrobiologi dan Laboratorium Kultur Sel dan Sitogenetika, Universitas Padjadjaran, Bandung pada November 2018–Januari 2019. Soyghurt dibuat dari susu kedelai yang difermentasi oleh Lactobacillus bulgaricus ATCC 11842. Jumlah koloni bakteri dihitung dengan metode total plate count (TPC) dan pH diukur dengan pH meter. Supernatan soyghurt dibuat dari soyghurt dan kemudian diintervensi ke dalam sel MEF dengan konsentrasi 1–20%. Viabilitas sel ditunjukkan dalam analisis penghambatan 50% (IC<sub>50</sub>). Pemberian supernatan soyghurt konsentrasi 1–20% menunjukkan tidak terdapat inhibisi proliferasi 50% (IC<sub>50</sub>). Namun, dari analisis morfologi, terdapat perubahan morfologi sel MEF pada kelompok yang diberi supernatan soyghurt dengan konsentrasi >12,5%. Efek mekanisme yang saling meniadakan dari fermentasi susu kedelai dengan probiotik diduga menjadi mekanisme hasil dari penelitian ini. Simpulan, intervensi supernatan soyghurt pada konsentrasi 1–20% tidak memiliki efek sitotoksik pada sel MEF, namun peningkatan konsentrasi supernatan soyghurt dapat meningkatkan potensi sitotoksik.

Kata kunci: Sel MEF, supernatan soyghurt, viabilitas sel

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# Introduction

Soybean is well known as a based plant food source for daily consumption. Besides protein, soy also contains fiber, iron, and lower level of free fatty acid. With technology development in food and dairy product, soybean is not only consumed as tofu and tempeh but also used as a raw material for fermented products. One of the fermented products produced from soy is soyghurt. The fermentation itself involved lactic acid bacteria, such as *Lactobacillus* sp. and *Streptococcus thermophilus*.<sup>1</sup>

Yogurt and probiotic have existed since Greece era. This processed food is used to be known as a functional food, that does not only contain a nutritional compound needed by a human but also have a beneficial effect on human health.<sup>2,3</sup> Some modification has been developed in the yogurt production process such as combined with additional natural resources as a raw material.<sup>1</sup> In this research, soybean used as a raw material in the soyghurt production process.

Fermentation of soymilk has excellent benefits for human health. Not only serves as an alternative type of beverage that can be consumed daily, but also able to be as an anticancer.<sup>4</sup> Probiotic as one of the critical components of soyghurt can inhibit proliferation and cytotoxic effect on the cancer cell line.<sup>5</sup> Another essential element for soyghurt is soybean, which contains phenolic compounds such as isoflavone, flavonoid, saponin, and quinone. These compounds also have a cytotoxic effect on the cancer cell line.<sup>6</sup>

Many studies have examined the effect of probiotic on the cancer cell line. However, there are no reports on the impact of yogurt on normal cell viability. A typical cell that often used in in vitro studies is the mouse embryonic fibroblast (MEF) cells. The MEF cells are the primary cell isolated from mouse embryonic. The MEF cell was used in many studies because these cells are easy to separate and fast to proliferate. Several studies that examined the cytotoxic effects of plant extracts on cancer cell line using MEF cells as a comparison of healthy cells.<sup>7–9</sup> This research was conducted to examine the impact of soyghurt supernatant intervention toward the viability of mouse embryonic fibroblast (MEF) cell.

# Methods

This study has used yellow soybean (*Glycine max*) that cultivated from Tasikmalaya, West

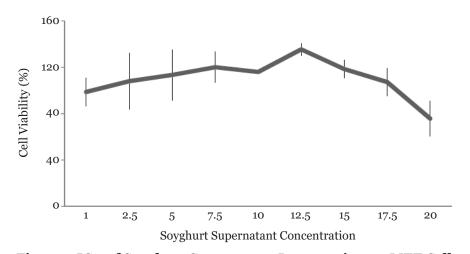
Java, Indonesia. The production of soyghurt from yellow soybean conducted in Microbiology Laboratorium and Cell Culture and Cytogenetic Laboratory, Universitas Padjadjaran, Bandung, Indonesia. The process of manufacturing, according to the previous research with some modification.<sup>1</sup>

First, soymilk made from yellow soybean. As much as 300 grams soybean washed and soaked in 5 L water that mixed with 0.25-0.5% sodium bicarbonate (NaHCO<sub>3</sub>) for 24 hours. Soybean then washed and peeled, and crushed with blender for 5 minutes then mixed with 2.5 L of hot water (80°C) until becoming a puree. Puree then filtered and added 125 grams sugar, sterilized at 121°C atm for 10 minutes. After that, 100 mL *Lactobacillus bulgaricus* ATCC 11842 was inoculated in soymilk then incubated in an incubator for 48 hours at 37–40°C.<sup>1</sup>

After incubation, an entire colony of bacteria from soyghurt calculated with total plate count (TPC) method.<sup>10</sup> The 1 mL of soyghurt diluted in NaCl ( $10^{-1}$ ,  $10^{-2}$ ,  $10^{-3}$ ,  $10^{-4}$ ,  $10^{-5}$ ,  $10^{-6}$ ).<sup>7</sup> Diluted soyghurt was cultured in the De Man, Rogosa, and Sharpe (MRS) agar. After 48 hours, the colony bacteria calculated. The pH of soyghurt examined by pH meter.<sup>1,2</sup> The bacterial colonies number obtained from this soyghurt in according to *Standar Nasional Indonesia*/SNI (Indonesian National Standards) 01-2981-1992. The characteristics of soyghurt produced include the colonies amounts were 2×10<sup>8</sup> CFU/mL, and acidity (pH) measured was 5.39.

Soyghurt supernatant made from soyghurt. Soyghurt centrifuged with 1,500 rpm T 4°C for 10 minutes. The supernatant harvested, then filtered using a 0.2  $\mu$ m syringe filter (Sigma-Aldrich).<sup>11</sup> After obtained the soyghurt supernatant, then phytochemical screening was conducted for further analysis about a compound that contained in soyghurt supernatant.

The MEF cell was isolated from mice embryo on the 10<sup>th</sup> day of gestational age according to previous protocol.<sup>12</sup> On the 10<sup>th</sup> gestational days, the pregnant mouse sacrificed, and the embryo was taken and washed with phosphate-buffered saline (Sigma-Aldrich). Head and visceral organ separated from the fetus. The embryo tissue was enumerated and added 0.25% trypsin-EDTA (Thermo Fisher Scientific) for 10 minutes until it becomes a single cell. Then, the cell was cultured in Dulbecco's modified Eagle medium (DMEM; Thermo Fisher Scientific) culture medium containing 1% antibiotic solution (Sigma-Aldrich)



**Figure 1** IC<sub>50</sub> of Soyghurt Supernatant Intervention on MEF Cell Data presented as mean±SD for three replication, soyghurt supernatant in X-axis, and relative cell viability in Y-axis

and 10% fetal bovine serum (Sigma-Aldrich). Then, soyghurt supernatant supplemented to MEF cells. From other study shown that bacteria supernatant with 10% concentration can inhibit the proliferation of cancer cell line.<sup>13</sup> Based on that result, the soyghurt supernatant concentration of 1% to 20% v/v chosen.

The cells were plated 96-well plate ( $5\times10^4$ ) for MTT assay examination. After confluence, cell was treated by soyghurt supernatant with various concentration (0%, 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% v/v), then incubated in incubator CO<sub>2</sub> T 37°C. After 24 hours, the viability cell examined using MTT assay method. Medium from the cell was taken out. MTT reagent 100 µL (5 mg/mL) added, then incubated for 2–4 hours in incubator CO<sub>2</sub> T 37°C until formazan crystal formed. After that, 200

Table Results of Yoghurt SupernatantPhytochemical Screening

Name of Compound	Results
Flavonoid	
Saponin	1
1	+
Polyphenol	-
Alkaloid	-
Sesquiterpenes/monoterpenes	+
Titerpenoid	-
Quinon	+
Tanin	-

 $\mu$ L MTT solvent (DMSO) added and formazan crystal as dissolved and the absorbance read at OD=450–550 nm. Measurements conducted and the concentration required for a 50% inhibition of viability (IC<sub>50</sub>) analyzed graphically. The standard graph plotted by taking the concentration of soyghurt supernatant in the X-axis and relative cell viability in Y-axis.<sup>14,15</sup>

The procedure of this study approved by the Health Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran, Bandung with letter number: 1268/UN6.KEP/EC/2018.

#### Results

Results of soyghurt supernatant phytochemical analysis contained saponins, sesquiterpenes/ monoterpenes, and quinones (Table).

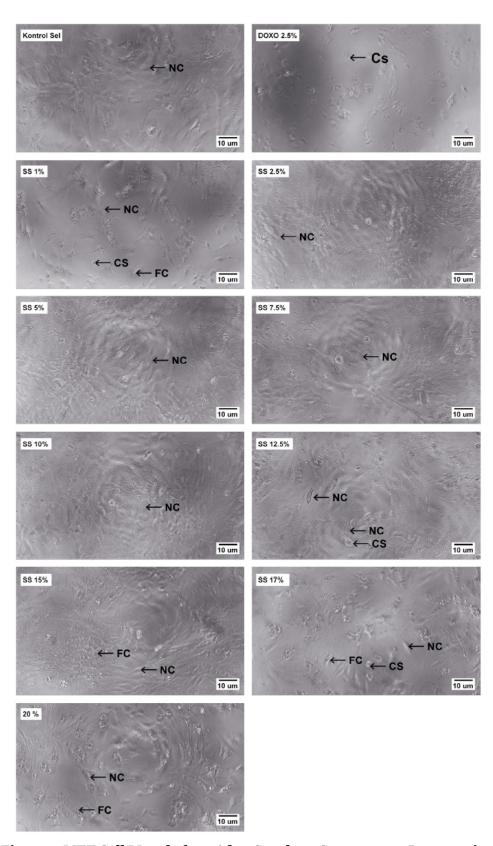
Figure 1 shows the intervention of the soyghurt supernatant at a 1-20% concentration has not reached a 50% inhibition of cell proliferation (IC<sub>50</sub>). However, when the dose increased, it showed a slight inhibition that is close to 20% proliferation of MEF cell.

Figure 2 showed morphological changing on MEF cell. The cells become dense, then shrinks, and fragmentation occurred at >12.5% soyghurt supernatant concentration compared to the control group. The morphological anomaly also showed in 1% concentration.

#### Discussion

In this study, animal milk substituted by soymilk

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**Figure 2** MEF Cell Morphology After Soyghurt Supernatant Intervention Observations using an Olympus inverted microscope (40× magnification). SS: soyghurt supernatant; NC: normal cell; CS: cell shrinkage; and FC: fragmented cell

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for fermentation. Soymilk has content that can be fermented by lactic acid bacteria for the bacterial growth process. This fermentation process produces higher antioxidant amount compared to unfermented soymilk.<sup>16</sup>

The probiotics used in the fermentation process produced the nutritional components needed for human health, such as proteins, vitamins, and antioxidant compounds.<sup>4</sup> In this study, a phytochemical screening test performed on the soyghurt supernatant, which used as an intervention in MEF cells. The result shows that the supernatant of soyghurt contains saponins, sesquiterpenes/monoterpenes, and quinones (Table). Saponins are a glycosides group found in plants and usually used to produce detergents.<sup>17,18</sup>

The density of the MEF cell observed after intervention with an increase in the concentration of soyghurt supernatant. The IC<sub>50</sub> (Figure 1) results showed that MEF cells did not experience the inhibition of proliferation up to 50% by soyghurt supernatant treatment with a concentration of 1–20% v/v. The different result directly obtained in the intervention of probiotics in cancer cells line, which showed proliferation inhibition and apoptosis. The case mechanisms include intrinsic and extrinsic apoptosis activation.<sup>17,18</sup> Previous studies showed that treatment on 100 µL doses of bacterial supernatant prevents cytokine-induced apoptosis in intestinal epithelial cells. Whereas in other research demonstrated that Lactobacillus supernatant doses >100 µL bacteria could inhibit proliferation of human colonic carcinoma cell line HT-29.13 Similar results showed from soybean extract treatment to cancer cells line.<sup>6</sup> In this study, it found that there was no proliferation inhibition until 50% population after intervention with sovghurt supernatant. We hypothesize that there is a counter mechanism presence caused by the combination of probiotics and soybeans. Our hypotheses that sovghurt has a mutually repealing mechanism that does not effect on MEF cell viability.

However, we observed that there were morphological changes at MEF cells with >12.5% concentration v/v. This result suspected because of the content of saponin in the soyghurt supernatant. Saponin is a glycosidic found in plants and has a detergent-like effect that can lyse cells walls such as blood cells and fungi. The active saponin ingredients are equivalent to Triton X that can be extracted from several plants and used as material to lyse fungi.<sup>17,18</sup> Moreover, we also suspect that cell morphological changes occurred because of quinone presence in the supernatant that has an antitumor effect.

Other studies report that the effect of saponins treatment in 4T1 cancer cells depends on the number of the dose. At low doses, the saponin compounds produced from ginseng will not inhibit cell viability, migration, and cell invasion, but in higher doses, it will inhibit cancer cell metastasis.<sup>19</sup> Different effects appear in neural cells; according to other studies, saponin has been shown to have the ability to support nerve cell embryo proliferation. In 3-4 days, with a dose of 100 ppm saponin will increase the number of nerve cells (42.89±5.90) compare to without saponin (19.22±6.67).<sup>20</sup> The difference in results depends on the characteristics of gene expression that interact with saponin compounds. This result showed that saponins treatment on endometrial cells could inhibit *miR-21-5p* gene and also have an apoptotic effect,<sup>21</sup> whereas in healthy neural cells, saponin support cell proliferation.<sup>20</sup> In this study showed that saponin which contained in soyghurt supernatant did not have a cytotoxic effect to MEF cells.

Beside saponins, the compounds that found in soyghurt are sesquiterpenes. Sesquiterpenes are terpenoid C15 composed of three isoprene units. Naturally, sesquiterpenes obtained in the hydrocarbon compound such as lactose and alcohol.<sup>22</sup> The structure of sesquiterpene that dominantly used in tumor treatment is a molecule with a ring structure, contain oxygen and carbonyl groups. This structure is called alpha-methylenegamma-lactone, or shortly called lactone sesquiterpenes. The structure of sesquiterpenes causes chemical changes that initiate damage to target cells or foreign microorganisms. In cancer cells, the protein activity will increase the sensitivity of the lactone sesquiterpenes to alkylate the membrane cell. This alkylation process will cause cell damage. Besides that, sesquiterpenes can regulate gene expression to activate and deactivate transcription factors on cancer cells.<sup>23</sup> Protein changes only useful in the cancer cell, while in healthy cells, the alkylation of cell walls will not appear. Furthermore, it will not trigger cell damage.

Other research showed that phenolic compound could stimulate the proliferation of cells, especially fibroblast cells. In the study accomplished by Nurulita et al.<sup>24</sup> demonstrated that apple extract containing phenolic compound

had a protective effect on NIH3T3 cells after  $H_2O_2$  induction. The similar discovery also found in the banana stem sap treatment in the wound healing process. The results have shown that flavonoid and derivatives contents can stimulate fibroblast cells proliferation in the wound healing process.<sup>25–27</sup>

## Conclusions

Soyghurt supernatant intervention at 1-20% concentration did not have a cytotoxic effect on MEF cell, but enhancement of soyghurt supernatant concentration can increase cytotoxic potential. For this reason, further research required for a complete understanding of the bioactive content of soyghurt and its mechanism regarding cell viability.

## **Conflict of Interest**

The authors declare no conflict of interests.

#### Acknowledgements

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# **RESEARCH ARTICLE**

# Validation of Patient Perception Instruments for Junior Doctor Performance: a Factor Analysis

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#### Abstract

The patient is an essential stakeholder within the medical healthcare system and an important stakeholder of the medical education program. The patients should be able to assess the performance of junior doctors in general practitioner residency to ensure their competency. Some instruments of patient assessment are available, but they do not adapt to local needs and context. This study aims to validate newly developed evaluation instruments from the patient's perspective against the performance of a junior doctor in a teaching hospital. Fifty patients from outpatient clinics of internal medicine of two teaching hospital Faculty of Medicine Universitas Islam Bandung were selected to fill out the questionnaire in September–October 2018. The tool consists of 20 items and used a 4-point Likert scale of strongly disagree, disagree, agree, and strongly agree. The SPSS version 21 have used to extract the data as the principal axis factoring of analysis. Oblimin rotation method was applied with Kaiser normalization to simplify and describe the data structure. The detailed analysis identified five factors based on the initial eigenvalue >1. Patient perception instruments of junior doctor performance (PIJDP) showed that five constructs extracted explained 81.27% of the variance of them. Constructs were namely: humanism, responsibility-accountability, communication-empathy, altruism, and pleasant manner. Construct validity achieved after the PIJDP run fifteen times, and consistency internal with Cronbach's alpha was 0.95. In conclusions, the PIJDP could be used to assess the performance of junior doctors and could make a novel contribution to the development of medical education.

Key words: Construct, evaluation, patient, performance, psychometric

# Validasi Instrumen Persepsi Pasien terhadap Kinerja Dokter Muda: Sebuah Analisis Faktor

#### Abstrak

Pasien merupakan stakeholder kunci dalam sistem pelayanan kesehatan dan stakeholder penting dalam program pendidikan kedokteran. Pasien dapat menilai kinerja dokter muda dalam pemagangan umum untuk memastikan kompetensi mereka. Beberapa instrumen penilaian pasien sudah dibuat, namun mereka tidak diadaptasi terhadap kebutuhan dan konteks lokal. Penelitian ini bertujuan memvalidasi instrumen evaluasi yang baru dikembangkan menurut perspektif pasien terhadap kinerja dokter muda di rumah sakit pendidikan. Lima puluh pasien dari klinik rawat jalan penyakit dalam dua rumah sakit pendidikan Fakultas Kedokteran Universitas Islam Bandung dipilih untuk mengisi kuesioner pada September–Oktober 2018. Kuesioner berisi 20 item yang menggunakan Skala Likert empat poin dari sangat tidak setuju, tidak setuju, setuju, dan sangat setuju. SPSS versi 21 digunakan untuk menganalisis data melalui principal axis factoring. Metode rotasi oblimin dengan normalisasi Kaiser diaplikasikan untuk menyederhanakan dan menjelaskan struktur data. Hasil analisis mengidentifikasi lima faktor berdasar atas eigenvalue awal >1. Instrument persepsi pasien terhadap kinerja dokter muda (PIJDP) menggambarkan 5 construct yang diekstraksi sebesar 81,27% dari varian indikator dapat dijelaskan oleh faktor yang terbentuk. Faktor tersebut adalah humanisme, tanggung jawab-akuntabilitas, komunikasi-empati, altruisme, dan sifat menyenangkan. Kesahihan construct dicapai setelah PIJDP diulang lima belas kali dan konsistensi internal dengan Cronbach's alpha sebesar 0,95. Simpulan, PIJDP dapat digunakan untuk menilai kinerja dokter muda dan dapat memberi kontribusi baru dalam pengembangan pendidikan kedokteran.

Kata kunci: Construct, evaluasi, kinerja, pasien, psikometrik

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#### Introduction

An instrument of the junior doctor's performance is necessary to assess the outcome of education. The result of education is one of the curriculum components in addition to the teaching method, assessment method, and the course content.<sup>1,2</sup> Patient satisfaction's questionnaire has been used to assess health services in a hospital. Assessment of patient satisfaction usually covers things relates to the hospital. They include clinical services, hour or day of operation, waiting time, friendliness of staff, amount of time with students officer and supervising doctor, lab services, and medication provided.<sup>3</sup> However, the assessment of the performance of a young physician taking a clinical clerkship program by the patients has not commonly performed. The patient is one of the key stakeholders within the medical curriculum, besides medical student, alumni, academic staff and employers.4

Evaluation of medical graduates' performance on the education needs assessment from the patient's perspective because they are the main stakeholder in a health care system.<sup>5</sup> Moreover, patient satisfaction is an essential aspect of the health care system to improve patient outcome. The success of health care services quality has determined by the satisfaction level of the patient as a user of the health provider.

The questionnaire is subjective measurement scales providing one or several scores based on sum (or mean) of responses to items (binary or ordinal variables). The construct validity is one of validation type that used to assess whether an instrument valid or not as a measurement tool. This validity obtained by conducting the exploratory factor analysis, and also can be used to evaluate the psychometric properties of an instrument.<sup>6.7</sup> Similarly, concurrent validity often was undertaken to validate the subjective measurement scale of the same matters from data of the other design. Validity refers to the degree to which a questionnaire measures the concepts of interest accurately.<sup>8</sup>

This study aims to validate newly developed evaluation instruments from the patient's perspective against the performance of a junior doctor in a teaching hospital.

#### Methods

The study used cross-sectional design for two

months in September–October 2018 in two teaching hospital of the Faculty of Medicine Universitas Islam Bandung; Al Ihsan Regional General Hospital and Al Islam Hospital. Al Ihsan Hospital is the primary referral hospital in the West Java province, Indonesia, while Al Islam Hospital is the type B hospital in Bandung city that serves both public patient and patient of insurance health coverage.

This study is part of the exploratory mixed method design, where the qualitative phase has already finished. From the qualitative finding, we achieved four themes in terms of humanism, responsibility, communication, and altruism. There is 2-factor analysis conducted, exploratory factor analysis (EFA) and confirmatory factor analysis (CFA).

Fifty patients at the outpatient clinic of internal medicine at two teaching hospital; Al Ihsan Regional General Hospital and Al Islam Hospital were selected to conduct an EFA. The sample size is determined based on a factor to participant ratio of 10:1, yielding 50 samples for five elements.

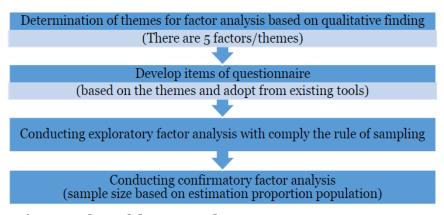
The 153 patients of Al Ihsan Regional General Hospital and Al Islam Hospital filled out the questionnaire of EFA result to conduct CFA. Determination of sample size based on the estimation proportion population as follows.

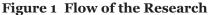
$$n = \frac{z_{1-\alpha/2}^{2}P(1-P)N}{d^{2}(N-1) + z_{1-\alpha/2}^{2}P(1-P)}$$

Notes: N: number of population, n: number of sample needed (sample size),  $z_{1-\alpha/2}$ : confidence interval 95% (1.96), P: anticipated population proportion of patient (0.54),<sup>9</sup> d: absolute precision required (0.07)

Based on the result of the qualitative finding, five variables have observed. The five variables are humanism, responsibility-accountability, communication, altruism, and pleasant attribute. The four patients of surgery inpatient clinic on the recovery phase was selected to conduct a focus group discussion (FGD) for 60 minutes in the primary teaching hospital of Faculty of Medicine Universitas Islam Bandung, Al Ihsan Regional General Hospital.

Figure 1 described the flow of the research. In determining whether the item on the instrument adequately represents the factor assessed, an exploratory structured analysis conducted. Fifty patients at the outpatient clinic of internal medicine at two teaching hospital were randomly selected to participate in this study. They were





asked to fill out the questionnaire that consists of 20 items using four-point of Likert scale, namely strongly disagree, disagree, agree, and strongly agree. The Kaiser-Myer-Olkin (KMO) statistic and Bartlett's test of sphericity were implemented to obtain sampling adequacy (factorability of the data).<sup>7</sup> The KMO value, which was above 0.6, showed an adequate sample and suggested suitable for factor analysis.<sup>10</sup> Using SPSS version 21, a principal axis factoring was conducted to simplify and describe the structure of data. An oblique rotation method, oblimin rotation with Kaizer normalization, performed to confirm the data extraction that grouped in the same factor. The early four factors or domains were humanism, accountability, excellence, and

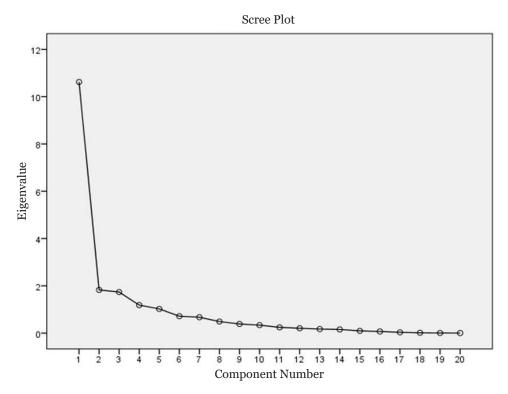


Figure 2 Factors in the 5 Components that Explained Variable based on the Initial Eigenvalue >1

altruism—the items with a higher value than o.6-factor loading grouped in the same factor or domain. Factor loading has been used to predict the correlation between factors and to determine the highest correlation factor.<sup>7,11</sup> The composition of the domains was five items of humanism, five issues of accountability, five elements of altruism, and five items of excellence.

Stages of scale development of the factor analysis included a) determining the construct of an instrument based on the qualitative finding on three themes, following competencies of skills as a doctor, communication ability, and professional behavior when serving the patient. The primary scales of the instrument has extracted from the result of FGD (4 patients of the surgery ward on the recovery phase). In this study, the development of questionnaires of patient perspective based on previous qualitative research. According to Creswell and Guetterman,<sup>12</sup> and Creswell,<sup>13</sup> qualitative findings could be used to develop an instrument of evaluation.

There are 4 subscales, altruism, humanism, accountability, and excellence based on article,<sup>6</sup> b) developing the 20 items of initial instrument onto 4 subscales which based on 4-point Likert scale, namely strongly disagree, disagree, agree, and strongly agree, c) completing the questionnaire by 50 patients of outpatient clinic of internal medicine at two teaching hospital of the Faculty of Medicine Universitas Islam Bandung. They are 18 patients of Al Islam Hospital. They were asked to rate items of questionnaire based on a 4-point Likert scale (from 1-strongly disagree to 4-strongly agree).

Confirmatory factor analysis was conducted to 153 patients at the outpatient clinic of internal medicine and surgery in two teaching hospitals. The 20 items of a patient perception instruments of junior doctor performance (PIJDP) was distributed to them to rate item based on a 4-point Likert scale and then analyzed by using the Linear Structural Relations (LISREL) program.

Collecting data used purposive convenience sampling until the quota of 50 samples reached. Data has collected in 1 September–30 October 2018 at two teaching hospital; Al Ihsan Regional General Hospital and Al Islam Hospital. The instrument used is a PIJDP as a result of scale development of EFA. For a sampling of CFA, it used purposive convenience sampling in two months from October to November 2018.

An EFA conducted using SPSS version 21. The data extracted by principal axis factoring method and oblimin rotation method. Before extracting the factor, the KMO and Bartlett's test of sphericity were tested respectively to get sampling adequacy and to determine the probability that correlations in a matrix are zero.<sup>10</sup> Some article gave that the sample size was determined based on factor and not variable. The sample size is ideally 10-20 participant per element,<sup>14</sup> but the minimum sample 30 to 100 can be accepted.<sup>12</sup> This study used 10 participants for five factors, yielding 50 participants. The total variance explained, and scree plots (Figure 2) were used to extract the factor. The total variance explained is in Table 1.

Confirmatory factor analysis used the LISREL program. The data confirmed for each factor and indicator variable of their construct. The item that had value more than 1.96 (t value>1.96) was

Factors	Initial Eigenvalues			Extraction Sums of Squared Loadings			Total of Rotation Sums
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	of Squared Loadings
1	10.621	53.104	53.104	10.621	53.104	53.104	10.621
2	1.828	9.141	62.245	1.828	9.141	62.245	1.828
3	1.736	8.680	70.925	1.736	8.680	70.925	1.736
4	1.186	5.928	76.853	1.186	5.928	76.853	1.186
5	1.025	5.124	81.977	1.025	5.124	81.977	1.025

Table 1 Total Variance Explained based on the Initial Eigenvalue >1

Factor 1: altruism; Factor 2: communication and empathy; Factor 3: pleasant manner; Factor 4: humanism and medical treatment; and Factor 5: responsibility-accountability

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		Factors				
Iter	ns	1	2	3	4	5
Q1	They are capable deal with my disease under supervision.	0.616				0.927
Q2	In serving patients, they do wholeheartedly until completely appropriate given the hospital authority.					0.800
Q3	The Ministry is done very nice.	0.517	-0.547			0.761
Q4	They are highly skilled and trained.	0.595				0.636
Q5	I do not hesitate against their ability in performing medical action standard.	0.673		0.564	-0.721	0.654
Q6	They are very friendly and enthusiastic when listening our complaints.		-0.842			0.652
Q7	They are very painstaking served us.	0.525	-0.895			0.501
Q8	They always give good advice related to our health.	0.600	-0.762	0.530		
Q9	They were polite when serving us.	0.553	-0.552	0.644		0.563
Q10	They know well the health problems we face.	0.865		0.524		0.595
Q11	During treatment, communication is easy to understand.	0.559	-0.709			0.508
Q12	Instructions given are clear and simple.	0.911	-0.574			0.639
Q13	They always involve our family in decision making during treatment if needed considerations of family.	0.781				
Q14	They look professionally serving us.	0.693	-0.500		-0.794	0.661
Q15	They are patient and friendly in serving us.	0.634	-0.691		-0.699	0.563
Q16	Young doctors always give precedence to the interests and our safety.	0.759		0.664		0.726
Q17	They do not hesitate to refer us when felt not his authority.	0.529		0.837		
Q18	I am pleased involved in research that they do for the development of medical science.			0.573		
Q19	I am not afraid of my complaints will be known by the other doctor.	0.564		0.928		
Q20	I served by them in ways that are fun.	0.870		0.666		0.639

# Table 2 Five Factors Solution based on Extraction Method of Oblimin Rotation of 50 Participants

Factor 1: altruism; Factor 2: communication and empathy; Factor 3: pleasant manner; Factor 4: humanism and medical treatment; and Factor 5: responsibility-accountability

considered significant and valid to describe its indicator constructed.

letter-number: 005/Komite Etik.FK/VI/2017.

# This study already had ethical approval from the Health Research Ethics Committee of Faculty of Medicine Universitas Islam Bandung with

## Results

Demographic information of EFA yielded 62% were males (n=31) and 38% were females (n=19). The average age was 51.96 years old in male respondent and 42.89 years old in the female

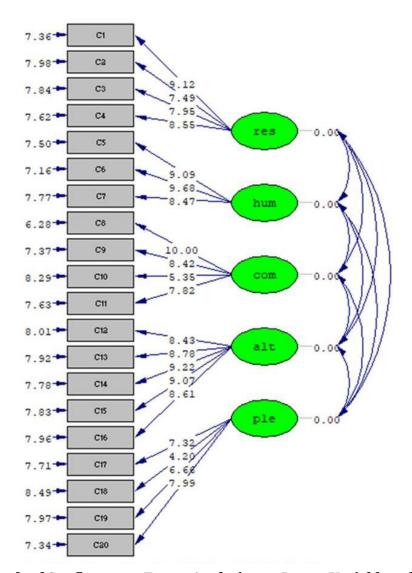


Figure 3 Result of Confirmatory Factor Analysis to 5 Latent Variables of 153 Patients

respondent. Demographic information of CFA resulted 44.44% were females (n=68), and 55.56% were males (n=85) with the mean of age was 53.97 years old.

As saw in Table 1, five factors had eigenvalue more than one. The factors that had eigenvalue more than one retained in this study. Then, the rotated component matrix was implemented to extract item in each factor.<sup>14</sup> Items inserted into each factor according to their values and nature. Items that had values more than 0.6 in every factor loaded at the same.<sup>11</sup>

Review of the factor structures suggested that 5 factors composition was the most appropriate

structure. The 5-factor solution initially showed a minimal cross loading and higher commonalities than the 4-factor solution. The KMO value was 0.810, and Bartlett's test of sphericity was 0.000 (p<0.001,  $X^2=1,018.134$ ) indicating sampling adequacy and significance of this construct validity. The minimum sample size of the performed analysis was 10:1 for the participant to factor ratio. The five factors at a 10:1 participant to factor ratio have been extracted, creating a sample size of  $50.^{14-16}$  Extraction of five elements composing 20 items of evaluation instruments showed 81.97% of the variance between them after 15 iterations (Table 1). Table 2 demonstrated

that items below were grouped based on factor loading value more than 0.6, except item q18 that has factor loading value 0.573. This result is following the study of Velicer and Fava<sup>17</sup> that item has a factor loading between 0.4 to 0.7 is low to moderate, and the item has a factor loading  $\geq$ 0.8 is considered high. The item has the factor loading <0.40 showed that that factor either not related to the other items. It might be an additional factor that should explore more.<sup>7</sup>

Based on the result of component number from the initial eigenvalue more than one, thus it was found five factors, namely 1) altruism, 2) communication and medical treatment, 3) a pleasant manner, 4) humanism, and 5) responsibility-accountability. The composition of factors was five items for altruism, four items for responsibility, four items for communication and medical treatment, four items for a pleasant manner, and three items for humanism.

Construct validity achieved after the PIJDP run fifteen times, and consistency internal with Cronbach's alpha was 0.95. The Cronbach's alpha value of each factor was: 0.948 of humanism, 0.947 of accountability, 0.947 of excellence, and 0.948 of altruism, which showed all factors have high reliability and can replicate for another study.

As shown in Figure 3, all items showed a significant relationship to each latent variable (responsibility-accountability, humanism and medical treatment, communication-empathy, altruism, and pleasant manner) with t value was almost similar (around 7–9). Every group of latent variables represented by item or indicator in that group (t value>1.96).

#### Discussion

The analysis resulted in 5 scales or factor, namely altruism, responsibility-accountability, communication skill, humanism, and pleasant manner. Central to understanding the essential factor in assessing performance seems to be represented by indicators within the latent variable (potential variable). The indicator representing for each scale as following: latent variable of responsibility-accountability was most represented by indicator item c1 (t value=9.12), "they are capable deal with my disease under supervision." It understood that the clinical clerkship student was still under supervision because their authority limited by regulation.

For the latent variable of the humanism and medical treatment, the most indicator represented with item c6 and c5 respectively (t value=9.68 and 9.09), which are an item of "they look professionally serving us" and item of "I do not hesitate regarding their ability in performing medical action standard." While latent variable of communication and empathy represented by item c8 (t value=10.0), "they are very friendly and enthusiastic when listening to our complaints." For the latent variable of altruism, the most indicator or observable variable represented by item c14 and c15. Item c14, if needed consideration of family in decision making during treatment, they always involve our family. Item 15, young doctor always giving the precedence to the interest and our safety. The last, latent variable was pleasant manner, this variable represented by item c20, I am not afraid the other doctor will know my complaints; and item c17, they were polite when serving us.

The evaluation of the performance of a junior doctor was a crucial aspect of the patient perspective. This study has developed a prototype instruments to evaluate the junior doctor's performance. This study used the participant to factor ratio of 10:1, thus create 50 of sample size. Amount of sample for an exploratory factor of analysis is ideally ten subjects for one item, but it depends on the purpose of research.<sup>18</sup> The instrument of this study was created to assess the performance of junior doctor from patients' perspective in terms of professional behavior, the particular aspects of the responsibility-accountability, the humanism, the communication, the altruism, and a pleasant manner. For principal component analysis, a factor with less than three items is generally weak and unstable, while factor with more than or the same as five items is strong.7 Almost all factors in this study categorized either as strong and strong enough, except the factor of altruism that consists of three pieces. It still accepted, since the factor that has three items were stable.

There were four items for responsibility, three items for humanism, four items for communication and medical treatment, five items for altruism, and four items for pleasant manner. Humanism refers to an entity consisting of respect for others, compassion, and integrity. In this questionnaire, humanism consists of trusted in performing a corrective action, professional, patient, and friendly. Responsibility at multiple levels refers to fulfilling the contract governing the doctor-patient relationship, the profession, and society. While altruism entails the consequence that the best interest of patient, not self-interest guide the doctors to do their job. Excellence involves a commitment to exceeding the ordinary expectations and the commitment to lifelong the learning.<sup>19</sup> The altruism of the questionnaire refers to some aspect, such as clear and straightforward instruction, involving family into decision making, give precedence to patient interest, know well problem of the patient, and fun services.

Communication skills have high clinical relevance. Studies have found that students' performances in communication increased the through time.<sup>20</sup> In this context, communication with the patients have some components, namely communication easy to understand, enthusiastic and friendly, painstaking in health service, and giving good advice of health. Doctor-patient communication is one aspect that increased adherence to medical treatment and enhanced clinical outcomes.<sup>9</sup> The element of the pleasant manner in the questionnaire refers to politeness in serving patients, known limitation and authority, involving in research, and trustworthiness.

Accordingly, research done by Donini-Lenhoff and Hedrick<sup>21</sup> shows that the ways of communication are an integrated pattern of learned beliefs and behaviors shared among groups. These include thoughts, styles of communicating, ways of interacting, views of roles and relationships, values, practices, and customs.<sup>22,23</sup> Therefore, communication skill is one of the essential factors that must be reserved by a physician in addition to clinical skill and professional behavior. This study is in line with Betancourt's<sup>22</sup> research showing that a doctor ought to has communication ability and clinical reasoning ability because evidence also suggests that doctor-patient communication highly linked to patient satisfaction and adherence and subsequently to health outcomes.

In this study, responsibility-accountability aspects assessed by knowing self-capability, able to deal with patient's disease, wholeheartedly whole serving, skillful, and trained. Studies assessing pertain to professionalism divided into three categories: as a part of the clinical program, as a comprehensive entity, and as separate elements of professionalism, such as humanism and ethical decision making.24 We conducted a study of assessing professionalism as a part of the clinical performance because it was done by determining aspects of being evaluated. Medical professionalism, in the performance context, is defined as the ability to meet the relationship-centered expectation required to practice medicine competently from the patient's perspective. Similarly, assessment of integrated inevitably have to be based on the patient evaluation in the workplace. The human assessment has three main fields of research in terms of bias and heuristic, original decision making, and social cognitive theory. Original decision making refers to how human can reach a satisfactory decision. The social cognitive theory stated decision making of individual highly influenced by the interpersonal and social environment. In other words, decision making depends on both the actual problem, motivation, and personal goal of the individual and local situation.25

Validity and reliability are an essential consideration to apply an evaluation tool. Based on the result of exploratory factor analysis, this instrument is acceptable as a tool of evaluation because this instrument was valid and reliable to assess the performance of junior doctor in a teaching hospital. This tool has similarities with the existing instrument developed by the American Board of Internal Medicine (ABIM) that consists of a component of altruism, humanism, accountability, and excellence. In other words, this result has construct validity based on exploratory factor analysis and concurrent validity based on the similarity with the existing instrument.<sup>24</sup> The results of Cronbach's alpha 0.95 indicates that the questionnaire is replicable for other research because of the value of Cronbach's alpha more than 0.7. Reliability determines reproducibility and consistency the result of measurement yields, and it is defined by a coefficient ranging from o; no reliability to 1; absolute reliability.8

#### Conclusion

The patient perception instruments of junior doctor performance (PIJDP) could be used to assess the performance of junior doctors and could make a novel contribution to the development of medical education.

#### **Conflict of Interest**

The authors have no conflict of interest to declare.

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