RESEARCH ARTICLE

DESCRIPTION AND FACTORS RELATED OF RISK ASSESSMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN COMMUNITY SETTING

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ABSTRACT

Background: Currently, Chronic Obstructive Pulmonary Disease (COPD) is one of degenerative disease with high morbidity and mortality, especially in low-income countries, including Indonesia. Increasing prevalence of COPD in Indonesia straightly correlates with increasing of tobacco smoking and air pollution level. Many studies had conducted to decrease COPD morbidity and mortality. Prevention is the best way to reduce the incidence of COPD. This study aimed to identify risk assessment of COPD in the community around Research, Teaching, and Clinical Unit (RTCU) Buaran, South Tangerang.

Methods: This study was cross sectional design and involved 134 respondents (41 males and 93 females) who live around RTCU Buaran, using two stages cluster sampling. During April to June 2015, respondents were

asked to fill the questionnaire that adapted from COPD Risk Screener that contains five questions.

Results: The study showed that the risk assessment of COPD of community around RTCU Buaran was 5.2% at high risk and 94.8% at low risk respectively. Using Fisher's Exact Test, there was significant correlation between the risk assessment of COPD and respondents' age, gender, the early symptoms of COPD, and tobacco smoking (p<0.05).

Conclusion: This study showed the risk assessment of COPD of community around RTCU Buaran was dominantly at low risk (94.8%), it seemed due to females' respondents more dominant than males'. Factors that significantly related to risk of COPD were age, gender, the early symptoms of COPD, and tobacco smoking.

Keywords: Chronic Obstructive Pulmonary Disease, risk factors, risk assessment, COPD Risk Screener.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of the biggest causes of death in the world. According to the World Health Organization (WHO), 65 million people suffer from COPD and more than 3 million people die from COPD. In 2002, COPD was categorized into five major diseases with high mortality rates. The mortality rate due to COPD is expected to increase by 30% within the next 10 years if there is no preventive action to reduce the habits that are the risk factors for COPD, especially cigarette consumption. WHO estimates COPD will fall into the category of three major diseases with high mortality rates by 2030. 1-3

In Indonesia, COPD is one of the main causes of death. The estimated prevalence of COPD in men aged \geq 30 years was 1.6% and in women 0.9 with an overall prevalence rate of 3.7%. The increasing prevalence of COPD in Indonesia is directly proportional to the increase of risk factors in the form of cigarette consumption rate, air pollution rate, and life expectancy.⁴

According to WHO, the main cause of COPD is smoking, both active and passive smokers. WHO estimates that in 2005 about 5.4 million people died from smoking. Deaths associated with cigarette consumption are projected to reach 8.3 million deaths per year by 2030. ^{1,5-6}

Some of the risk factors for COPD besides cigarettes are age, air pollution, chemical compounds in the form of gas. Although smoking is a major cause of COPD, data obtained from WHO suggest that about 400,000 deaths per year are due to exposure to the remaining fuel gas. ^{1,3}

COPD is an irreversible, progressive chronic disease. Treatment for COPD disease is given to reduce symptoms and improve the quality of life of patients. However, COPD is a preventable disease. WHO mentioned that prevention measures that can be done is to prevent exposure to risk factors for COPD cause.^{3,6}

Efforts to prevent COPD in Indonesia itself is still lacking. There are no special programs or programs conducted by health institutions to prevent COPD. According to the Indonesian Pulmonologist Association (PDPI), prevention is in the form of efforts to avoid cigarette

smoke, air pollution, recurrent airway infections, and recognize the initial symptoms of COPD.⁷

Prevention such as avoiding secondhand smoke for active or passive smokers can be one effective prevention because active smokers in Indonesia is still quite a lot, especially in the age of 30-34 years of 33.4% and more in men. In addition to cigarette smoke, the incidence of recurrent respiratory infections can also be a risk factor that should be prevented because the incidence of airway infections in Indonesia is 25%.⁴

Assessment of the risk level for COPD in this study is expected to be a source for individuals to control or avoid exposure to risk factors and more familiar with early symptoms of COPD so that the incidence of COPD will be increasingly reduced each year.

This study aimed to describe the extent of the risk of COPD on the guided community at RTCU Buaran and to know the relationship between exposure to risk factors and early symptoms to the level of risk that the study subjects had.

MATERIALS AND METHODS

The type of this research is descriptive-analytic quantitative research using cross sectional design. This research was conducted in RT 001/003, RT 001/004, and RT 003/005 in the Guided Community of Research, Teaching, and Clinical Unit (RTCU) Buaran, Faculty of Medicine and

Health Sciences, Syarif Hidayatullah State Islamic University Jakarta. This research was conducted in April to June 2015. The population reached in this research is the community in RT 001/003, RT 001/004, and RT 003/005 in the Guided Community of RTCU Buaran who is more than 35 years in 2015.

To determine the sample size, this study used the following formula:

$$n1 = n2 = \frac{(Z\alpha\sqrt{2PQ} + Z\beta\sqrt{P1Q1 + P2Q2})^{2}}{(P1 - P2)^{2}}$$

Explanation:

n = Number of samples required

 $Z\alpha$ = Alpha standard deviation on confidence interval 95% with two way hypothesis that is equal to 1,96

 $Z\beta$ = Beta standard deviation on confidence interval 80% that is equal to 0,84

P1 = The proportion of COPD events that were affected by age \geq 60 years was 0.714.

P2 = The proportion of COPD events that was affected by age <60 years was 0.286.

P = Total Proportion: (P1+P2)/2

Q1 = 1-P1

Q2 = 1-P2

Q = 1-P

$$n1 = n2 = \frac{(1,96\sqrt{2(0,5)(0,5)} + 0,84\sqrt{(0,714)(0,286) + (0,286)(0,714)})^{2}}{(0,714 - 0,286)^{2}}$$

$$n1 = n2 = \frac{(1,386 + 0,537)^{2}}{0,183}$$

$$n1 = n2 = 20,20218$$

The sample used for this study based on the calculation of the sample size is 20 people in each group so that the minimum total sample size is 40 people.

This study uses two stage random sampling. The initial election is selecting RW under the guidance of RTCU Buaran. From the selected RW then one RT in each RW will be picked. Residents from each RT were selected randomly as many as 40 people.

Inclusion Criteria

- People living in the guided area of RTCU Buaran
- Age of the respondent above 35 years old
- Never been diagnosed with COPD

Exclusion Criteria

- People who refused to be respondents

This study uses a questionnaire that has been developed from COPD Risk Screener to assess the level of one's risk to Chronic Obstructive Pulmonary Disease. Chronic Obstructive Pulmonary Disease Population Screener (COPD-PS) is a validated questionnaire, it can be used for people who have never been diagnosed with COPD. The COPD-PS questionnaire contains five questions which are the most common questions asked to diagnose COPD (questionnaire is shown in the table 1).⁵

Assessment of questionnaires that have been filled using the scores contained in the questionnaire. If the score is 5 or more then the individual is already at high risk for COPD. A score of 5 or more of the results of this COPD-PS questionnaire has a sensitivity of 84.4% and a specificity of 60.7%. Although the results of the specificity are small but

with high sensitivity this may determine the patient for further examination of spirometry. Validation was performed not only in patients attending the lung clinic in the United Satates, but also performed on the general community using an online survey.⁵

Respondents who had been selected with two stage cluster sampling were approached by researchers who conducted guided interviews with five questions on the adapted COPD Risk Screener. After guided interviews, the results are included into the scores contained in the COPD Risk Screener to test the validity and reliability of 30 respondents and then analyzed by univariate and bivariate analysis. Data that have been collected from respondents will be processed using SPSS software version 20.

Univariate analysis was used to describe the characteristics of independent and dependent variables. The entire data contained in the questionnaire is processed and presented in the form of frequency distribution tables. Bivariate analysis is used to see the relation between independent variable and dependent variable by using Chi-Square test analysis, if Chi-Square test requirement is not fulfilled, Fisher Exact test will be used. This research has passed the ethical review and its implementation has passed the informed consent.

Table 1. COPD-PS questionnaire items

No	Questionnaire items
1	During the past 4 weeks, how much of the time
	you feel short of breath?
2	Do you ever cough up any "stuff", such as mucus
	or phlegm?
3	Please select the answer that best describes you
	in the past 12 months. I do less than I used to
	because of my breathing problems.
4	Have you smoked at least 100 cigarettes in your
	entire life?
5	How old are you?

RESULTS AND DISCUSSION

Validity and Reliability Test Results

Validity and reliability test is done in RTCU Buaran area with 30 respondents. Respondents consisted of 18 women and 12 men with an average age of 50 years. This validity and reliability test data processing uses SPSS version 20.

An item in the instrument can be said to have good validity if the Pearson Correlation result is greater than a simple correlation coefficient (table r). Table r used in this validity test is worth 0.361 with N=30 and a significance level of 1%.

Table 2. Result of validity test on questionnaire items

No.	Questionnaire Items	Pearson Correlation	P Value (2-tailed)	Table r	Interpretation
1.	Shortness of breath in the last 4 weeks	0.795	<0.001	0.361	Good
2.	Sputum and mucus when coughing	0.829	<0.001	0.361	Good
3.	Limited activity baecause of breathing problems during the past 12 months	0.761	<0.001	0.361	Good
4.	Smoker	0.707	< 0.001	0.361	Good
5.	Age	0.523	0,003	0.361	Good

The results of the validity test questionnaire items asked in this study indicate that all items that have good validity. All items of the questionnaire can be incorporated into the questionnaire to determine the risk assessment that refers to the Risk Screener COPD questionnaire.

Table 3. Result of reliability test

Cronbach's Alpha	Number of item
0.768	5

The results of Cronbach's Alpha from the reliability test stated that the questionnaire instrument used in this study is 0.768. If included in the criterion of Cronbach's Alpha value interpretation division then the instrument belongs to a strong reliability criterion.

Table 4. Qustionnaire items reliability test result

No.	Questionnaire Item	Cronbach's Alpha if item deleted	Interpretation
1.	Shortness of breath in the last 4 weeks	0.548	Good
			_ ,
2.	Sputum and mucus	0.556	Good
	when coughing		
3.	Limited activity	0.568	Good
	because of		
	breathing problems		
	during the past 12		
	months		
4.	Smoker	0.680	Good
5.	Age	0.784	Good

From the results of reliability tests on item questionnaire, it was found that the reliability of each item questionnaire is strong. This means that the questions given to the respondent are constant or stable. Each item contained in the questionnaire will be included in the questionnaire for the purposes of scoring and data analysis. Some questions

will be added to anticipate the confusion of respondents.

Characteristic description of respondents

Characteristics of respondents of this study is illustrated through the distribution of respondents by sex, age, occupation, and level of education.

Table 5. Distribution of respondent characteristics (N=134)

Variable	Category	N	%
Sex	Male	41	30.6
	Female	93	69.4
Age	35-59 year old	109	81.3
	≥ 60 year old	25	18.7
Employment	Employed	46	34.3
	Unemployed	88	65.7
Level of education	Low	76	56.7
	Middle	56	41.8
	High	2	1.5
Smoker	No	100	74.6
	Yes	34	25.4

From table 5, it was found that male respondents amounted to 41 people (30.6%) and female respondents amounted to 93 people (69.4%).

Respondents in the age range 35-59 years were 109 people (81.3%) while respondents aged over 60 years were 25 people (18.7%). Age of all respondents according to inclusion criteria, which is more than 35 years.

Respondent's work was divided into two categories, namely employed and unemployed. Forty-six respondents (34.3%) were employed while 88 respondents (65.7%) were unemployed.

The level of education of the respondents was divided into three categories, namely the low, middle and high. The group included in the low level of education category were those who did not attend school, did not finish primary school, and graduated from elementary school. The group included in the middle level of education category was the respondent who has graduated from junior high school and graduated from high school. The groups included in the high

level of education category were respondents who have graduated from college or have bachelor degree. From the table above, 76 respondents (56.7%) were included in the low level of education category, 56 respondents (41.8%) were included in the middle level of education category, and 2 respondents (1.5%) were highly educated.

Table 5 showed that 100 respondents (74.6%) are not smokers, while 34 other respondents (25.4%) consume cigarettes. The number of non-smoker respondents was bigger than smokers can be due to more female respondents.

An overview of early symptoms of COPD on respondents

The variables of COPD symptoms in this study were taken based on the symptoms that were included in the item of the Risk Screener COPD questionnaire. These symptoms were symptoms of COPD that can be detected as early as possible so that respondents can avoid factors that have risk of causing COPD.

Table 6. Distribution of early symptoms of COPD on respondents (N=134)

Variable	Category	N	%
	Never	114	85.1
	Rarely	11	8.2
Shortness of breath	Several times	2	1.5
	Often		2.2
	At any time	4	3.0
	Never	53	39.6
	When having Acute	70	52.2
	Respiratory Infection		
	Some days every month	4	3.0
Sputum production	Everyday	7	5.2

Limited activity because of breathing problems	Strongly Disagree Disagree Unsure Agree	65 49 4 13	48.5 36.6 3.0 9.7
problems	Agree	13	9.7
	Strongly Agree	3	2.2

From table 6, it was found that 114 respondents (85.1%) never experienced shortness of breath, 11 respondents (8.2%) rarely experienced shortness of breath, 2 respondents (1.5%) several times experiencing shortness of breath, 3 respondents 2.2%) often experienced shortness of breath, and 4 respondents (3.0%) experienced shortness of breath at any time.

From table 6, it was found that 53 respondents (39.6%) never produce sputum or mucus, 70 respondents (52.2%) produced sputum only when getting upper respiratory tract infection, 4 respondents (3.0%) produced sputum only a few days every month, and 7 respondents said everyday produced sputum.

From table 6, it was found that as many as 65 respondents (48.5%) stated strongly disagree if their activity was disturbed by breathing problems, 49 respondents (36.6%) disagreed, 4 respondents (3.0%) unsure, 13 respondents (9.7%) agreed, and 2 respondents (2.2%) stated strongly agreed if their activity was reduced due to breathing problems felt. The data in table 7 was resulted from the risk

Description of COPD risk level among respondents

Tablel 7. Distribution of COPD risk to respondents (N=134)

Level of risk	N	%
Low risk	127	94,8
High risk	7	5,2

factors and symptoms contained in the questionnaires that have been summed according to the scoring rules on the COPD Risk Screener. The results of the assessment are divided into two categories, namely low risk and high risk for the occurrence of COPD.

A total of 127 respondents (94.8%) were included in low risk category, while 7 respondents (5.2%) were included in high risk category for the occurrence of COPD.

Bivariate Analysis

The test performed for bivariate analysis is Fisher's because all distribution variables are abnormal and the requirement of chi-square test is not fulfilled because the number of the expected count <5 is at >33% cell where it should only be <20% cells.

The independent variables used were gender, age, symptoms and risk factors of COPD to be analyzed against dependent variable ie risk level of COPD. If p-value is <0.05 then there is a significant difference between independent and dependent variable, with confidence interval 95%.

Table 8. Relationship between respondent characteristics and COPD early symptom to risk level (N=134)

Variables -	COPD r	isk level	Total	P value
v ariables -	Low	High		P value
Male	35	6	41	0.003
Female	92	1	93	
35-59 y. o	106	3	109	0.023
≥ 60 y. o	21	4	25	
Employed	86	3	89	0.224
Unemployed	41	4	45	
No short of breath	123	2	125	< 0.001
Had short of breath	4	5	9	
No limited activity	116	2	118	< 0.001
Limited activity	11	5	16	
Mucus (-)	121	2	123	< 0.001
Mucus (+)	6	5	11	
Non smoker	99	1	100	< 0.001
Smoker	28	6	34	

Table 8 showed that 8 men having a high risk of COPD, while only 1 woman having high risk. In contrast, 92 women had a lower risk compared to men who only amounted to 35 respondents. This result had significant difference with p value = 0.003.

From table 8, it was found that the number of high-risk COPD respondents with \geq 60 years of age was 4 people compared with respondents with age 35-59 years as many as 3 respondents. In contrast, respondents aged 35-59 years with a low risk of COPD were 106 people, more than respondents aged \geq 60 years of 21 respondents. This result had significant difference with p value = 0.023.

Table 8 performed the number of high risk respondents who employed were 3 people, while high-risk respondents who were unemployed amounted to 4 people. In contrast, low-risk respondents who were employed amounted to 86 people, higher when compared to low-risk respondents who are unemployed with 41 people. This result has no significant difference with p value = 0.224.

Table 8 showed that the number of high-risk respondents who have experienced symptoms of shortness of breath were 5 people, more than high-risk respondents who never experienced symptoms of shortness of breath, that was as much as 2 people. Conversely, the number of low-risk respondents who never experienced symptoms of shortness were as many as 123 people, more than respondents with low-risk who have experienced symptoms of shortness of breath. This result had significant difference with p value <0.001.

According to table 8, it was found that the number of high-risk respondents who agreed if their activities are disturbed due to breathing problems were 5 people, more than high-risk respondents who do not agree if the activity was interrupted by breathing problems amounting to 2 respondents. In contrast, low-risk respondents who disagreed if their activities were disturbed by respiratory problems amounting to 116 people, more than low-risk respondents who did not agree if the activity was disrupted due to breathing problems that amounted to 11 respondents. This result was significantly difference with p value <0.001.

Table 8 performed that high risk respondents who agree if you feel always produce mucus/sputum amounted at 5 people, more than high-risk respondents who were not agree if they always produce mucus/sputum amounted to 2 respondents. Conversely, low-risk respondents who did not agree if they feel always produce mucus/sputum amounted at 121 people, more than low-risk respondents who agree if they always produced sputum that amounted to 6 respondents. This result was significant difference with p value <0.001.

Table 8 showed that high risk respondents who smoke

amounted to 6 people, while high risk non-smoking respondents amounted to 1 person. Conversely, low-risk non-smokers were 99 people while low-risk respondents who smoked were 28 respondents. This result was significantly difference with p value <0.001.

DISCUSSION

This study performed that respondents who had low risk of COPD was higher than who had high risk of COPD. There were some reasons of this result, first, based on respondent characteristics that average age in this study was 49 years. Second, manjority of respondent was female that assumed had no smoking behavior or non smoker. Some studies supported these reasons stated that primary prevention of COPD from an early age is necessary because as age increases, the risk for higher COPD coupled with an inadequate lifestyle such as smoking can lead to an increased risk of COPD. ⁶⁻⁹

Bivariate analysis showed some interesting results. This study found that there was significantly difference between individual aged before and after 60 years old and regarding COPD risk level. Based on research conducted by Rycroft ¹⁰ that the deaths caused by COPD are mostly on individuals aged 65-74 years. This result also explained by Akkermans¹¹ in his study that the prevalence of individuals diagnosed with COPD through spirometry examination is an elderly individual. According to Akkermans¹¹, there is a significant correlation between age with incidence of COPD (p value <0,001).

Not significant results between employed and unemployed status to COPD risk level occured because this study did not include the type of work of the respondent. This type of work greatly affects the risk of COPD because there are some jobs that have direct exposure to air pollution. Air pollutant substances is one of the causes of chronic inflammatory processes in cases of COPD.

As expected, the early symptoms of COPD (shortness of breath, limited activity due to brathing problems, and mucus production) had significantly relation to COPD risk level. These results were reinforced by research conducted by Roberto de Marco⁸ which stated that the initial symptoms caused by respiratory hyper-responsiveness have a significant relationship to the incidence of COPD. Respiratory hyper-responsiveness has manifestations of shortness of breath and increased mucus production. Respiratory hyper-responsiveness is one of the cardinal signs of bronchial asthma, but if this process occurs chronically, irreversible tissue damage causes COPD. ^{3,7,8,12,13}

Respondents who felt their respiratory tract filled with phlegm or mucus had a risk factor for COPD. Phlegm is a secretion of goblet cells of the respiratory tract due to an inflammatory process that occurs. Production of phlegm or mucus due to chronic inflammatory processes leads to narrowing of the lumen of the airways. This results in a decrease in oxygen intake when an individual performs physical activity. This decrease in oxygen intake will make the patient having shortness of breath when doing physical activity. ^{8,10,13}Thus they had to limit their daily activities.

In addition to age, cigarette consumption is the biggest risk factor for COPD. Substance contained in cigarette smoke is the cause of inflammation of the respiratory tract. Prolonged exposure to secondhand smoke can cause chronic inflammation that causes COPD. ^{8,10,13}

Based on research conducted by Rycroft¹⁰ that 2.3% to 8.4% of deaths caused by COPD, the proportion of men is greater than the proportion of women with age range 65-74 years. Although cigarette consumption may explain the difference in proportion between men and women, further research is required to explain the difference in proportions without affecting factors such as cigarette consumption. ^{10,13,14}

These study resulted that between smoker and non smoker was significantly difference to COPD risk level. The study from Akkermans¹¹ had similar result which states that there was significant relationship between cigarette consumption and the incidence of COPD (p value = 0,006). Based on research conducted Agusti¹² it was mentioned that cigarette consumption is the main cause of chronic inflammatory process which is the pathophysiology of COPD.

Advantages of study

Chronic obstructive pulmonary disease is a degenerative disease that has modifiable risk factors. If an individual is diagnosed with COPD, treatment is only useful for relieving exacerbations. Interventions to prevent COPD are by reducing exposure to the main causes of COPD. This study was conducted to assess the level of individual risk for COPD. The sooner an individual is identified as having a risk for COPD, the easier it is to reduce the incidence of COPD.

This research was also conducted on the community. The population caught in this study can describe the frequency of individuals who have a high risk of COPD.

COPD Risk Screener is a questionnaire to identify an individual's risk of COPD. This questionnaire has been used in various countries and has been through the validation process for this research.

Study limitations

This study had several limitations. Most of the respondents have low education and are elderly, so that there were some questions that are not understood by the respondents.

We included only 134 respondents in one district, it quite small amount for community study.

CONCLUSION

Based on the result of this research, the conclusion is as follows: in the guided community of RTCU Buaran in 2015, the distribution of risk of COPD was: high risk at 5.2% and low risk at 94.8%. There was a significant association between sex, age, initial symptoms of COPD, and smoking behavior with a risk level of COPD with p value <0.05 There was no significant association between employed status and risk level of COPD with p value = 0,224.

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REFERENCES

- World Health Organization, 2014. Chronic Obstructive Pulmonary Disease. [Cited 26 Oct 2014] Available from : www.who.int/tobacco/research/copd/en/index.html.
- COPD International, 2014. COPD Statistics. [Cited 26
 Oct 2014] Available from: http://www.copd-international.com/library/statistics.html.
- 3. Raherison C, Girodet PO. (*Review*) Epidemiology of *COPD*. EurRespir Rev. 2009;18:114,213-221.
- Halbert RJ, Natoli JL, Gano A, Badamgraw E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. EurRespir J. 2006;28:523-532
- Martinez, F. J., Raczek, A. E., Seifer, F. D., Conoscenti, C. S., Curtice, T. G. & D'Eletto, T., et al. Development and initial validation of a self-scored COPD Population Screener questionnaire (COPD-PS). COPD: Journal of Chronic Obstructive Pulmonary Disease. 2008;5:2,85-95.
- Karen D, Gerrad WF. Identifying chronic obstructive pulmonary disease in primary care of urban underserved patients: tools, applications, and challenges. J Natl med Assoc. 2010;102:570-578.
- Ralph S, RS Williams. Prospective medicine: the next health care transformation. Acad Med. 2003;78:1079-1084.
- 8. De Marco R, Accordini S, Marcon A, et al. *Risk factors for Chronic Obstructive Pulmonary* Disease *in a European cohort of young adults*. American Journal of Respiratory and Critical Care Medicine. 2011:Vol 183.
- 9. Mosenifar Z, Kamangar N, Byrd RP. Chronic Obstructive Pulmonary Disease Clinical Presentation.

- [Cited 18 Jul 2015]. Available from: http://emedicine.medscape.com/article/297664-clinical
- 10. Rycroft CE, Heyes A, Lanza L, Becker K. *Epidemiology* of chronic obstructive pulmonary disease: a literature review. International Journal of COPD. 2012;7:457-494.
- 11. Akkermans RP, Biermans M, Robberts B, terRiet G, Jacobs A, van Weel C, Wensing M, Schermer T. *COPD Prognosis in Relation to Diagnostic Criteria for Airflow Obstruction in Smokers*. EurRespir J. 2014;43:54-63.
- 12. Agusti AGN, Noguera A, Sauleda J, Sala E, Pons J, Busquets X. (Review) Systemic effects of chronic obstructive pulmonary disease. EurRespir J. 2003;21:347-360.
- 13. Patriani, Ana A., Paramastri I., Priyanto, M.A., 2010. Pemberdayaan keluarga dalam rehabilitasi medic paru pada penderita penyakit paru obstruktif kronik di Balai Pengobatan Penyakit Paru-Paru Yogyakarta. Yogyakarta: Berita Kedokteran Masyarakat.
- 14. Spruit MA, Singh SJ, Garvey C, et al. An Official American Thoracic Society/European Respiratory Society Statement: Key Concepts and Advances in Pulmonary Rehabilitation. American Journal of Respiratory and Critical Care Medicine. 2013:Vol 188