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Article

Smoking from a Younger Age is the Dominant Factor in the Incidence of Chronic Obstructive Pulmonary Disease: Case Control Study

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Abstract: Background: Indonesia ranks the 7th largest in the world in the number of deaths caused by cigarettes including those caused by Chronic Obstructive Pulmonary Disease (COPD). The purpose of this study was to determine the influence of initial smoking age and habit on the incidence of COPD. Methods: This research was case control study. The sampling in this research was systematic random sampling method. The samples of this study were 56 respondents of a case group and 56 respondents of a control group. This study was conducted at Ngudi Waluyo Hospital, Wlingi, Blitar in October until November 2017. Results: Factors that influenced the incidence of COPD were male (p=0.00; OR=6.333; 95%CI=2.776 – 14.450), smokers who initially smoked at < 15 years old (p=0.00; OR=11,769; 95%CI=4.086 – 33.903), smokers (p=0.013; OR=3.273; 95%CI=1.291–8.2999), smokers (p=0.00050; OR=5.1318; 95%CI=1.9004 – 13.8958), initial smoking habit at the age of <15 years old (OR=12; CI=1,346-106,950), initial smoking habit at the age of ≥ 15 years old (OR=3,647; CI=1,625-8,183), and smoking duration ≥ 30 years (OR=8,857; CI=3,298-23,787). Conclusion: There are three factors of smoking behavior that influence COPD which are smoking habit, initial smoking age, and smoking duration, but initial smoking habit at the age of <15 years old has the biggest risk than another (OR=12; CI=1,346-106,950).

Keywords: chronic obstructive pulmonary disease, initial smoking age, smoking habit, smoking duration.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a non-communicable disease whose number of incidence worldwide increases from year to year (1). COPD is a major source of morbidity, mortality, and costs in the Western world (2). In the world, currently the number of people with COPD reaches 384 million and it is estimated that this number will continue to increase and become the third leading cause of death in the world by 2030 (3). The burden of chronic respiratory diseases is generally increasing across the globe, and COPD is one of the main causes of mortality and morbidity (2).

The main risk factor for COPD is smoking (3). Another study stated that cigarette smoking is the leading cause of COPD in the United States (4). The pathogenesis of smoking-related COPD includes the protease, anti-protease, and oxidant-antioxidant hypotheses and abnormal repair processes (Johns et al., 2014). COPD disease caused by smoking is usually initiated by injury lung. Smoking habit is the cause of 8 out of 10 cases of COPD (6). More than 75% of COPD cases has lung injury caused by a long period of smoking (7).

Another risk factors that can influence COPD were the presence of other environmental exposures such as exposure to biomass fuels and air pollution, and host factors such as age, sex, or socioeconomic status (3,8). Age is often listed as a risk factor for COPD. It is because of all vital organs lose their function with age, hence the decline in lung function which occurs progressively after about 25 years of age. In the case of COPD the age factor plays a role in increased cell aging, stem cell fatigue, increased oxidative stress, changes in the extracellular matrix and a reduction in endogenous anti-aging molecules and protective pathways such as autophagy (9). In the past, most studies have shown that prevalence and mortality of COPD is higher in men than women, but based on recent studies in developed countries reported that the prevalence of COPD in men and women is almost the same. This may be due to changes in smoking behavior patterns (10).

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1st reviewer:
The title is perhaps a little misleading and should probably say "Smoking from a Younger Age is the Dominant Factor in the Incidence of Chronic Obstruction Pulmonary Disease: Case Control Study" because it is likely to be a combination of smoking early with young lungs and then the younger one starts the longer the exposure to the toxins in the lungs.

Author:
Ok I already revise it

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3rd reviewer:
Chronic obstruction pulmonary disease" in Title, which is different to the text " Chronic obstructive ….".

Author:
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3rd reviewer:
The abbreviation of "COPD"is appeared in the first line of the text (page1, Introduction line 1). Following this sentence, the authors should use "COPD" alone, instead of "chronic obstructive pulmonary disease (COPD

Author:
Ok, we already revise it

COPD is the first cause of disability in the world (11). Limited ability to perform daily activities occur in 3 of 4 cases suffering from COPD (12). The disease also limits a person's ability to climb stairs (13). Early retirement occurs in 40% of patients with COPD (14). In Europe, COPD accounts for 50% of total health funds each year and causes productivity loss of € 48.4 billion (15). In the United States, it is estimated that COPD costs USD 50 billion consisting of direct cost as much as USD 30 billion and indirect cost as much as USD 20 billion (16). It is estimated that there are 12 million people suffering from COPD and each year, 120.000 of them die annually (17). In Indonesia, COPD resulted in a loss of productive age (Total Daily Loss) of 901,744 and medical expenses of IDR 1,294,165,188,810 and the 6th cause of death on a national scale (18). Therefore, it is necessary to make a preventive effort to reduce the prevalence of COPD in order to reduce the number of deaths due to COPD, so the purpose of this study was to determine the influence of initial smoking age and habit on the incidence of COPD.

Health is a human right mandated by the 1945 Constitution of the Republic of Indonesia, therefore there is a need for protection against the effects of cigarette smoke, especially for people who are not active smokers in accordance with Health Law No. 36 of 2009 article 115 concerning the establishment of a No Smoking Zone policy. (KTR) as a form of government efforts to protect the public in the public environment. Based on 2013 basic health research data, out of 38 districts/cities only 9 districts/cities implemented the No Smoking Area (KTR) policy in East Java Province (19).

Blitar district is one of the districts in East Java that has not implemented this regulation in 2018. On the other hand, one of the diseases caused by smoking, namely COPD, has a fairly high prevalence compared to other diseases. The prevalence of COPD in Blitar District, East Java is 3.7 percent (19). Based on the recapitulation of patient data at Ngudi Waluyo Wlingi Hospital, Blitar District in 2016, the morbidity rate of COPD inpatients was ranked tenth with 226 patients, while for outpatient care, COPD was ranked thirteenth with 953 patients (18). The main risk factor for COPD is exposure to cigarette smoke. 36.3% of the total population aged ≥ 10 years in Blitar District have a history of smoking habits, with 30% still actively smoking until now. In Blitar District, the average number of cigarettes smoked per day per person in 2013 was 9.7 cigarettes (19).

2. Material and Methods

2.1. Study Area

This study takes place in Ngudi Waluyo Wlingi Hospital, Blitar District, Indonesia. Indonesia is the country in the world with the 7th highest number of deaths due to COPD, while Blitar district is one of the districts in East Java, Indonesia that does not have regulations regarding smoking-free areas, so the prevalence of smoking-related diseases is quite high in Blitar District, one of which is COPD. The prevalence of COPD in Blitar District, East Java Indonesia is 3.7 percent (19). Ngudi Waluyo Wlingi Regional Hospital was designated as a Regional Public Service Agency (BLUD) Hospital in Blitar which is a teaching hospital that has 16 accredited services, so this hospital is a suitable place for research. Based on the recapitulation of patient data at Ngudi Waluyo Wlingi Hospital, Blitar District in 2016, the morbidity rate of inpatient COPD was ranked tenth with 226 patients, while for outpatient care, COPD was ranked thirteenth with 953 people (20).

2.2. Data Source

This research was analytical observational study using case control design. This research was conducted in April - December 2017 at Ngudi Waluyo Hospital in Wlingi, Blitar, East Java, Indonesia. The case group was people who had been diagnosed as suffering from COPD, while the control group was people who had never been diagnosed as suffering from COPD.

2.3. Sample Selection

The sampling used in this study was systematic random sampling. The case population in this study were all patients with COPD aged ≥30 years at Ngudi Waluyo Wlingi Regional Hospital, Blitar District, East Java. The diagnosis of COPD is determined based on the doctor's diagnosis on the patient's medical record. While the control population in this study were all patients aged ≥ 30 years who did not have a history of COPD based on medical records at Ngudi Waluyo Wlingi Regional Hospital, Blitar District, East Java. The sample size was calculated using Lemeshow's comparison case which generated 56 samples in each group (1:1). The samples were divided into case group and control group. The case group consisted of samples with COPD, while the control group consisted of samples without COPD. The cases and control were taken randomly using systematic random sampling technique. The control group was selected based on the current age of the respondent, namely at least 30 years. Systematic random sampling in both the case and control groups based on the serial number of patients seeking treatment at the Ngudi Waluyo Hospital with multiple numbers based on the number of patients receiving treatment divided by the number of samples needed then the sample was taken based on the multiple of the results of the distribution in the sampling frame.

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2nd Reviewer:
Authors reviewed an old topic with already known pathophysiological associations, yet non new info have been added to what is already known since last 3-4 decades. In this view also the aim of the study should be better exposed

Author:
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3rd reviewer:
The authors state that the age and sex are host factors that can influence COPD (page1, Introduction, line 16-17). However, in this study, the age and sex of Control group are significantly different (p=0.00) those of Case (COPD) group. The age and sex in control group should adjust to Case group

Author:
We are sorry, we are don't quite understand about what you mean, in this research we already limited the age which is ≥30 years, can you give some example or advise, so that we know what do you mean? Thank you so much

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1st Reviewer:
1.the other personal characteristics and smoking behaviours are described in the manuscript. But are fairly blunt measures.

Author:
Im sorry I don't quite understand about what do you mean. Please if you have better advise to categorize or describe this? Thank you

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1st reviewer:
We are not giving any detailed information about the case definition for COPD in this study (section 2.2). Nor can we determine who are the cases. This needs to be provided, so that we can understand how well the case definition identifies COPD

Author:
We add about this in 2.3 section.
We definite the COPD based on doctor diagnosis in medical record

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Ages. Section 2.3 says not younger than 30 years of age but later says that controls were 20 years or older. So this needs to be clarified.

Author:
Ok. We already revised it

2.4. The Operational Definition of the Variable

The dependent variable studied is COPD, while the independent variables studied divided into two groups which are characteristics of respondents (age, sex, job, and education), and smoking behavior (smoking habits, early smoking age, and duration of smoking). Determination of COPD status in the case group using medical records while in the control group using a questionnaire. The age variable is determined by the result of the reduction between the interview date and the respondent's date of birth and is grouped into two categories, namely adult ($\geq 30 - < 65$ years old) and elderly (≥ 65 years old). The sex variable is divided into two, namely male and female. The education variable is divided into two, namely low education (no school up to junior high school) and higher education (senior high school to college).

The smoking habit variable was divided into three variables, namely non-smokers (never smoked), smokers (people who have smoked at least 100 cigarettes in their lifetime and in the environment where they live and work there are no smokers), and smokers who were exposed to secondhand smoke (smokers who are other than exposure to cigarette smoke itself, also exposure to cigarette smoke from other people). The variable of initial smoking age was divided into three groups, namely non-smokers, Smokers who initially smoked at < 15 years old, and smokers who initially smoked at ≥ 15 years old. The variable of smoking duration was divided into three groups, namely non-smokers, smokers who smoked for < 30 years, and smokers who smoked for ≥ 30 years.

2.5. Instruments

Data collection using a questionnaire instrument and using secondary data which is patient medical records. The questionnaire used in this study was the modification of the basic health research and non communicable disease research. The questionnaire was on participant's smoking habit and status in relation to COPD. The questionnaire had been tested to 20 participants in order to obtain the validity and realibility.

2.6. Statistical Analysis

The collected data were then analyzed descriptively and analytically using computer assistance. Data processing used bivariate analysis using the confidence of interval 95% ($\alpha = 0.05$).

2.7. Ethical Clearance

All participants were provided with written informed consent approved by Ethics Commission of Faculty of Public Health, Universitas Airlangga (certificate number: 536-KEPK).

3. Results

3.1. Characteristics of Respondents

Table 1 presents about the distribution of respondent characteristics and their effects on the incidence of COPD. It showed that from a total of 112 respondents. The majority of COPD patients are male (75%), including in the elderly age group (53.57%), and have low educational background (67.86%). Significant results showed at male (p=0.00; OR=6.333; 95%CI=2.776 – 14.450), which means that male had 6.33 times greater risk than female. Significant results also showed at elderly group (p=0.00; OR=11,769; 95%CI=4.086 – 33.903) which means that the elderly group had 11.769 times greater risk than respondents in adult group.

Table 1. Characteristics of Respondents

Variables	Case		Control		*p*	OR	95% CI
	n	%	n	%			
Sex							
Male	42	75.00	18	32.14	0.00	6.333	2.776 – 14.450
Female	14	25.00	38	67.86			
Age							
Elderly (≥ 65 years old)	30	53.57	5	8.93	0.00	11.769	4.086 – 33.903
Adult ($\geq 30 - < 65$ years old)	26	46.43	51	91.07			
Education							
Low Education	38	67.86	36	64.29	0.69	1.173	0.536 – 2.567
High Education	18	32.14	20	35.7			
Total	56	100.00	56	100.00			

3.2. Smoking Behavior

Table 2 presents about the distribution of respondents' smoking behavior and its effect on the incidence of COPD. It showed that from a total of 112 respondents, 55 of them were smokers and 57 other respondents were non smokers. Of the non smokers, 29 of them were exposed to secondhand smoke.

Table 2. Smoking Behavior of Respondents

Variables	Case		Control		p	OR	95% CI
	n	%	n	%			
Smoking Habit							
Non Smokers	8	14.28	20	35.72			
Secondhand Smokers	11	19.64	18	32.14	0.236	1.5278	0.5028 – 4.6418
Smokers	37	66.07	18	32.14	0.00050	5.1318	1.9004 – 13.8958
Initial Smoking Age							
Non Smokers	19	33.93	38	67.86			2.599 – 13.620
Smokers who initially smoked at < 15 years old	6	10.7	1	1.79	0.026	12	1.346 – 106.95
Smokers who initially smoked at ≥ 15 years old	31	55.4	17	30.35	0.002	3.647	1.625 – 8.183
Smoking Duration							
Non Smokers	19	33.93	38	67.86			
Smokers who smoked for < 30 years	6	10.71	11	19.64	0.881	1.091	0.350 – 3.401
Smokers who smoked for ≥ 30 years	31	55.36	7	12.5	0.000	8.857	3.298 – 23.787
Total	56	100.00	56	100.00			

Significant results showed at smoking habit variable, smokers had 5.1318 times greater risk of developing COPD compared with non-smokers (p=0.00050; OR=5.1318; 95%CI=1.9004 – 13.8958). On other hand, Secondhand smokers had no influence on the incidence of COPD (p=0.236; OR=1.5278; 95%CI=0.5028 – 4.6418). Significant results also showed at initial smoking age variable, smokers who initially smoked at <15 years old had 12 times greater risk of developing COPD compared with non-smokers (p=0.026; OR=12; 95%CI=1.346 – 106.95), while smokers who initially smoked at ≥ 15 years old had 3.647 times greater risk of developing COPD than non-smokers (p=0.002; OR=3.647; 95%CI=3.298 – 23.787). Smoking period of less than 30 years had no influence on the incidence of COPD (p=0.881; OR=1.091; 95%CI=0.350 – 3.401), whereas smoking period of more than 30 years was influential. Smokers who smoked for more than 30 years had 8.857 times greater risk of developing COPD compared with non-smokers (p=0.000; OR=8.857; 95%CI=3.298 – 23.787) (Table 2).

4. Discussion

4.1. Key Findings

Factors that influenced the incidence of COPD were male (p=0.00; OR=6.333; 95%CI=2.776 – 14.450), elderly group (p=0.00; OR=11,769; 95%CI=4.086 – 33.903), smokers (p=0.00050; OR=5.1318; 95%CI=1.9004 – 13.8958), initial smoking habit at the age of <15 years old (p=0.026; OR=12; 95%CI=1.346 – 106.95), initial smoking habit at the age of ≥ 15 years old (OR=3,647; CI=1,625-8,183), and smoking duration ≥ 30 years (OR=8,857; CI=3,298-23,787).

4.2. Characteristics of Respondents

The current study showed that the OR value of elderly group is higher than adult group (p=0.00; OR=11,769; 95%CI=4.086–33.903). This is in line with previous studies in Sousse, Tunisia in 2013 on elderly> 70 years (p = 0.007; OR = 10,403; 95% CI = 2,072–52,222), V € astra G€otal and inWest Sweden and Norrbotten in Northern Sweden at 2008-2012 in elderly ≥60 years (OR = 8.40; 95% CI = 3.70 - 19.1), and based on the results of Indonesian basic health research in 2013 for elderly ≥60 years (OR = 4.5; 95% CI = 7.6 - 8.2) (21–23). The three previous research results have similar results, namely the elderly group has the highest risk of suffering from COPD than other age groups.

The current study showed that the OR value of male group is higher than female group (p=0.013; OR=3.273; 95%CI=1.291–8.2999). This is in line with previous studies in Sousse, Tunisia in 2013 on male group (p=0.010; OR=0.198 95%CI=0.062–0.635), in Anhui, China in male group (OR=2.01; 95%CI=1.22 – 3.33), and based on the results of Indonesian basic health research in 2013 for male group (OR=1.3; 95%CI= 4 – 4.3) (21,22,24,25). The four previous research results have similar results, namely the male group has the highest risk of suffering from COPD than

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Table 3 seems out of place in this manuscript. Rather than provide the information in tabular form, I suggest the researchers convey the important information in words. For example, the case definitions are needed to understand COPD in these study to understand the relationship with the risk factors. So a narative style will be more useful to the reader.

Author:
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1st reviewers:
It would be preferable to read whether this information will be received in Indonesia? Will there be public health campaigns to address these health risks? What can these limited results be used for in Indonesia.

Author:
Ok, I already revise it

female groups. The difference in ORs in each study both in age and sex criteria can be caused by several things such as differences in the methods used, the number of samples taken, and the bias from other risk factors that influence.

4.3. Smoking Behavior

4.1.1. Smoking Habit

The current study showed that the OR value of smokers group is higher than another group (p=0.00050; OR=5.1318; 95%CI=1.9004–13.8958). This is in line with previous studies in Abeshge district, Southern Ethiopia, 2019 on smokers group (OR=4.19; 95%CI=2.59–6.78) (8). Two previous studies in Sousse, Tunisia and Anhui, China that describe in more detail about the smoking group show that current smokers have a higher risk than former smokers (21)(25). When compared with three previous studies, the OR value of smoking habit variable in this study is higher than in other studies. This is because the methods used in this study are different, and the number of samples is smaller. However, there is a similarity that smokers group have a greater risk of suffering from COPD than non-smokers group. Smoking cigarette in a long period disrupts ciliary movement, inhibits alveolar macrophage function and ultimately leads to hypertrophy and hyperplasia of the mucus excreting gland (26). Cigarette smoke contains many species of reactive oxygen (free radicals), which deplete antioxidant mechanism resulting in tissue damage and potentially leading to COPD (27).

4.1.2. Initial Smoking Age

Initial smoking habit at the age of <15 years old has the biggest risk than another (OR=12; CI=1,346-106,950). There is a significantly higher risk of starting smoking at <15 years of age than $\geq$ 15 years old which is from 3.647 to 12. This is due to smoking in childhood and adolescence can slow down the growth and development of the lungs, thereby increasing the risk of incidence of COPD during adulthood. This is due to the fact that the lungs still grow and develop until the age of 20 years. Smoking as early as before the age of 20 years causes one's lungs unable to develop optimally both in terms of ability and function. This kind of lungs fail to work properly, produce breath that tends to be short and will be problematic when used to exercise or perform physical activity. Although the health of people who quit smoking will increase dramatically compared with their health when they smoke, some cases of lung damage at an early age due to cigarettes are irreversible (28). Therefore, it is necessary to implement policies regarding age restrictions that are allowed for the purchase of cigarettes, especially for mobile cigarette sellers as well as cross-sector cooperation in health, education or other government sectors in socializing the dangers of smoking from an early age.

4.1.3. Smoking Duration

Smokers who smoked for more than 30 years had 8.857 times greater risk of developing COPD compared with non-smokers (p=0.000; OR=8.857; 95%CI=3.298 – 23.787). The results for the length of smoking < 30 years are not in line with another studies which show that smoking has an effect, namely, someone who has a smoking habit > 20 years is more likely to develop COPD 3-4 times compared to someone whose smoking habit is $\leq$20 years (29). This is influenced by exposure to cigarette smoke from other people, namely from 55 respondents who smoke, 26 of them are also exposed to cigarette smoke from other people, so this is what disturbs the results of the study. On the other hand, the results of smoking duration of $\geq$ 30 years are in line with other literature which also states that the longer the smoking habit, the greater the risk of developing COPD (30).

5. Conclusion

Starting age for smoking at less than 15 years old has the highest risk (OR=12; CI=1,346-106,950) for COPD. The other factors that influenced the incidence of COPD were male (p=0.00; OR=6.333; 95%CI=2.776 – 14.450), elderly group (p=0.00; OR=11,769; 95%CI=4.086 – 33.903), and smoking duration $\geq$ 30 years (OR=8,857; CI=3,298-23,787).

Abbreviations
The following abbreviations are used in this manuscript:

COPD   Chronic Obstructive Pulmonary Disease
USD   United Stated Dollar
BLUD   Regional Public Service Agency (in English)
OR   Odds Ratio
CI   Confidence Interval

References

1.   Global Initiative for Chronic Obstructive Lung Disease. Pocket guide to COPD diagnosis, management, and prevention: a guide for health care professionals 2017 report. Germany: Global Initiative for Chronic Obstructive Lung Disease, Inc; 2017. 1–33 p.
2.   Ehteshami-Afshar S, FitzGerald JM, Doyle-Waters MM, Sadatsafavi M. The global economic burden of asthma and chronic obstructive pulmonary disease. Int J Tuberc Lung Dis. 2016;20(1):11–23.
3.   Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2018 report [Internet]. Germany: Global Initiative for Chronic Obstructive Lung Disease, Inc; 2018. 1–44 p. Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2015_Apr2.pdf
4.   Wheaton AG, Liu Y, Croft JB, VanFrank B, Croxton TL, Punturieri A, et al. Chronic Obstructive Pulmonary Disease and Smoking Status — United States, 2017. MMWR Morb Mortal Wkly Rep. 2019;68(24):533–8.
5.   Johns DP, Walters JAE, Haydn Walters E. Diagnosis and early detection of COPD using spirometry. J Thorac Dis. 2014;6(11):1557–69.
6.   U.S. Department of Health and Human Services. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease. Atlanta: U.S. Department of Health and Human Services, Inc; 2010. 792 p.
7.   U.S. Department of Health and Human Services. The health consequences of smoking-50 years of progress. Atlanta: Centers for Disease Control and Prevention; 2014.
8.   Woldeamanuel GG, Mingude AB, Geta TG. Prevalence of chronic obstructive pulmonary disease (COPD) and its associated factors among adults in Abeshge District, Ethiopia: A cross sectional study. BMC Pulm Med. 2019;19(1):1–9.
9.   Mercado N, Ito K, Barnes PJ. Accelerated ageing of the lung in COPD: new concepts. Thorax. 2015 May;70(5):482–9.
10. Landis SH, Muellerova H, Mannino DM, Menezes AM, Han MLK, van der Molen T, et al. Continuing to confront COPD international patient survey: Methods, COPD prevalence, and disease burden in 2012-2013. Int J COPD. 2014;9:597–607.
11. Murray CJL, Barber RM, Foreman KJ, Ozgoren AA, Abd-Allah F, Abera SF, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. Lancet [Internet]. 2015;386(10009):2145–91. Available from: http://www.sciencedirect.com/science/article/pii/S014067361561340X
12. Jones PW, Brusselle G, Dal Negro RW, Ferrer M, Kardos P, Levy ML, et al. Health-related quality of life in patients by COPD severity within primary care in Europe. Respir Med. 2011;105(1):57–66.
13. Vermeire P. The burden of chronic obstructive pulmonary disease. Respir Med. 2002;96(Suppl.3):S3–10.
14. Fletcher M, Molen T Van Der, Barnes N, Walsh J. COPD : The new workplace epidemic. 2011;(September):1–21.
15. European Lung White Book. The economic burden of lung disease: the cost of respiratory disease [Internet]. Europe: European Respiratory Society; 2011 [cited 2020 Feb 27]. p. 1–2. Available from: https://www.erswhitebook.org/chapters/the-economic-burden-of-lung-disease/the-cost-of-respiratory-disease/
16. WHO. Chronic obstructive pulmonary disease (COPD) [Internet]. 2017 [cited 2020 Feb 27]. p. 208–12. Available from: https://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)
17. May SM, Li JTC. Burden of chronic obstructive pulmonary disease: healthcare costs and beyond. Allergy Asthma Proc. 2015;36(1):4–10.
18. Ministry of Health RI. Perilaku merokok masyarakat Indonesia. Jakarta: Ministry of Health RI; 2014. p. 1–11.
19. Ministry of Health RI. Laporan riset kesehatan dasar (Riskesdas) tahun 2013 [Internet]. Jakarta; 2013. Available from: http://www.depkes.go.id/resources/download/general/Hasil Riskesdas 2013.pdf
20. RSUD Ngudi Waluyo Wlingi. Laporan Kasus Morbiditas di Rumah Sakit Ngudi Waluyo Wlingi Tahun 2016. Blitar District; 2017.
21. Daldoul H, Denguezli M, Jithoo A, Gnatiuc L, Buist S, Burney P, et al. Prevalence of COPD and tobacco smoking in Tunisia - Results from the BOLD study. Int J Environ Res Public Health. 2013;10(12):7257–71.
22. Kusumawardani N, Rahajeng E, Mubasyiroh R. Association of cigarrete smoke exposure and chronic obstructive pulmonary disease (COPD) in Indonesia. J Ekol Kesehat. 2017;15(3):160–6.

23.   Hagstad S, Backman H, Bjerg A, Ekerljung L, Ye X, Hedman L, et al. Prevalence and risk factors of COPD among never-smokers in two areas of Sweden - Occupational exposure to gas, dust or fumes is an important risk factor. Respir Med. 2015;109(11):1439–45.

24.   Jaganath D, Miranda JJ, Gilman RH, Wise RA, Diette GB, Miele CH, et al. Prevalence of chronic obstructive pulmonary disease and variation in risk factors across four geographically diverse resource-limited settings in Peru. Respir Res [Internet]. 2015;16(1):1–9. Available from: http://dx.doi.org/10.1186/s12931-015-0198-2

25.   Zha Z, Leng R, Xu W, Bao H, Chen Y, Fang L, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in Anhui Province, China: a population-based survey. BMC Pulm Med. 2019;19(1):1–10.

26.   Isselbacher, Braunwald, Wilson, Martin, Fauci, Kasper. Prinsip-prinsip ilmu penyakit dalam. 13th ed. Asdie HA, editor. Jakarta: EGC; 2000.

27.   Kumar V, Abbas A, Aster J. Buku ajar patologi robbins. 7th ed. Ham M, Saraswati M, editors. Netherlands: Elsevier; 2015. 369–375 p.

28.   U.S. Department of Health and Human Services. Let's make the next generation tobacco-free : your guide to the 50th anniversary Surgeon General's report on smoking and health [Internet]. Atlanta: U.S. Department of Health and Human Services, Inc; 2014. 20 p. Available from: https://bookstore.gpo.gov/products/health-consequences-smoking-50-years-progress-report-surgeon-general-full-report-epub-ebook

29.   Puspitasari S. Hubungan antara kebiasaan merokok dengan kejadian penyakit paru obstruksi kronik (PPOK) di RS Paru Jember [Internet]. Universitas Jember; 2012. Available from: https://repository.unej.ac.id

30.   Alsagaff H, Mukty A. Penyakit obstruksi saluran napas: dasar-dasar ilmu penyakit paru. Surabaya: Airlangga University Press; 2009.