ORIGINAL RESEARCH

ANALYSIS OF RISK FACTORS AFFECTING THE OCCURRENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN INDONESIA

Analisis Faktor Risiko Yang Mempengaruhi Kejadian Penyakit Paru Obstruksi Kronis di Indonesia

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a lung disease caused by the occurrence of air flow limitation in the lungs and also causes 60% of all deaths in Indonesia. Purpose: This study aimed to analyze the risk factors that affect the incidence of COPD in Indonesia. Methods: This study was conducted in July–August 2019 in Indonesia as an analytic research study with a cross-sectional design, using data from the Indonesia Family Life Survey-5. The sample consisted of respondents aged >15 years, giving a total of 34,231 respondents. Data analysis was partially carried out using the chi-square test to analyze the relationships between the variables. Results: The majority of respondents were female, were aged <40 years, and had a low level of education. Risk factors for the development of COPD included, among others, an age of >40 years (p = 0.02; PR = 1.20; 95% CI = 1.02–1.41), male gender (p = 0.01; PR = 1.26; 95% CI = 1.07–1.49), smoking (p = 0.01; PR = 1.22; 95% CI = 1.03–1.44), first smoking age < 40 years (p = 0.02; PR = 1.22; 95% CI = 1.03–1.44), residence in urban areas (p = 0.01; PR = 1.43; 95% CI = 1.20–1.70), being underweight (p = 0.01; PR = 2.17; 95% CI = 1.76–2.66). Conclusions: The risk factors that affect the incidence of COPD include being aged >40 years, being male, smoking, taking up smoking when aged <40 years, urban residence, and being underweight.

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ABSTRAK

Pendahuluan: Penyakit Paru Obstruksi Kronis (PPOK) adalah...
INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by persistent respiratory symptoms and airflow limitation due to clogged airways and alveolar abnormalities or disorders caused by noxious particles or gases (Global Initiative for Chronic Obstructive Lung Disease, 2018). It is a condition that can be prevented and treated. Chronic obstructive pulmonary disease (COPD) underdiagnosis was found in all surveys and may account for > 90% of cases determined by spirometry (Lamprech et al., 2015). Incidence rates of COPD continue to increase despite spirometry tests for early detection in children at primary school (Vogelmeier et al., 2017).

According to the 2015 Global Burden of Disease report, there was an increase in the death rate from COPD by nearly 11% and the prevalence of COPD by 44% from 1990 to 2015. If action is not taken, it could potentially be the third most prevalent cause of death globally in 2030 (Soriano et al., 2017). It is one of the four most severe non-communicable diseases (NCDs) that account for 60% of deaths in Indonesia (Ministry of Health RI, 2019).

Riskesdas findings in 2013 showed that the prevalence of COPD in Indonesia among people aged >30 years was 3.70%, with the highest prevalence rate in the province of East Nusa Tenggara (10%) and the lowest in Lampung (1.40%). The average age of COPD patients was 56 (+11.30), 55.8% of patients were women, and 22.90% were smokers (Lamprech et al., 2015).

Bangladesh has a higher prevalence of COPD among rural residents than urban residents, in males than females, among people aged >40 years, among people with a lower level of education, among those with underweight body mass index (BMI) values, and among those with a history of smoking (Alam, Chowdhury, Siddiquee, Ahmed, & Clemens, 2015). Smoking is a key external risk factor for the development of COPD, while secondary and tertiary factors are exposure to dust in the workplace, to smoke, and to noxious fumes. Indoor air pollution from the combustion of biomass fuels and outdoor air pollution can interact with individual factors, which can also increase the incidence of COPD (López-Campos, Tan, & Soriano, 2015). In line with this, Viniol & Vogelmeier (2018) research also highlights that the risk factors and triggers of COPD include smoking, air pollution, and respiratory limitations.

The incidence of the disease is still high in Indonesia, but research data about COPD still limited. One source showing COPD rates in Indonesia is Indonesia Basic Health Research (Riskesdas) 2013; however, in 2018, Riskesdas published no data concerning COPD. COPD is a

penyakit paru yang disebabkan oleh adanya keterbatasan aliran udara di paru yang juga menyebabkan 60% kematian di Indonesia. **Tujuan:** Penelitian ini bertujuan untuk menganalisis faktor risiko yang mempengaruhi kejadian PPOK di Indonesia. **Metode:** Penelitian ini dilakukan pada bulan Juli-Agustus 2019 di Indonesia, merupakan penelitian analitik dengan desain cross-sectional, menggunakan data dari Indonesian Family Life Survey-5 (IFLS-5). Sampel yang diambil adalah responden yang berusia > 15 tahun yang berjumlah 34.231 responden. Data dianalisis dengan uji chi-square untuk menganalisis hubungan antar variabel. **Hasil:** Mayoritas responden berjenis kelamin perempuan, berusia < 40 tahun, dan berpendidikan rendah. Faktor risiko terjadinya PPOK diantaranya yaitu usia responden > 40 tahun (p = 0,02; PR = 1,20; 95%CI = 1,02-1,41), jenis kelamin laki-laki (p = 0,01; PR = 1,26; 95%CI = 1,07-1,49), merokok (p = 0,01; PR = 1,22; 95%CI = 1,03-1,44), usia pertama merokok (p = 0,02; PR = 1,22; 95%CI = 1,03-1,44), tempat tinggal di perkotaan (p = 0,01; PR = 1,43; 95%CI = 1,20-1,70), dan underweight (p = 0,01; PR = 2,17; 95%CI = 1,76-2,66). **Kesimpulan:** Faktor risiko yang mempengaruhi kejadian PPOK diantaranya adalah usia > 40 tahun, berjenis kelamin laki-laki, merokok, usia pertama merokok < 40 tahun, bertempat tinggal di perkotaan, dan underweight.
type of NCD, and NCDs account for 60% of deaths in Indonesia; therefore, the current research utilized Indonesian Family Life Survey 5 (IFLS-5) big data that is available for researchers for free. IFLS-5 was conducted in Indonesia in 2014–2015 by RAND in collaboration with Survey Meter (Strauss, Witoelar, & Sikoki, 2016). The purpose of the current study was to analyze the risk factors that affect the incidence of COPD in Indonesia.

METHODS

This study used a cross-sectional design. The data resource analyzed in this study is the IFLS-5 report. The IFLS is a sustainable demographic and health survey that was first conducted in 1993, and its fifth round (IFLS-5) was carried out in 2015. The community survey in IFLS 5 collects data on households, individuals, and communities using multistage stratified sampling. The sampling frame in the first survey, namely in 1993, was based on the household level with an area of 321 households (20 households were randomly selected from urban and 30 from rural areas). Households in 13 of Indonesia’s 27 provinces were selected, representing 83% of Indonesia's population in 1993. IFLS-5 was approved by the ethical review board of RAND and the University of Gajah Mada in Indonesia (Strauss, Witoelar, & Sikoki, 2016). At the household level, household members were randomly selected to provide detailed individual information. The IFLS-5 gathered data from 36,377 respondents, and 34,262 respondents age >15 years were asked whether a medical professional had diagnosed one of their relatives with COPD. Of these, 618 respondents answered “yes,” and 33,613 answered "no" (Figure 1).

The measurements used in IFLS-5 included anthropometric measurements and questionnaire items regarding age, gender, education, occupation, smoking, age of quitting smoking, age of first smoking, smoking when ill, and residence condition. Height was measured in millimeters using a plastic seca board (model 213), and weight was measured in kilograms using a model Camry EB1003 scale. BMI was calculated as weight in kilograms divided by height in meters squared, and the results were classified into underweight (<18.5 kg/m²), normal (18.5–22.9 kg/m²), overweight (23–24.9 kg/m²), and obese (>25 kg/m²) (Liu, Zeng, Hong, Li, & Fu, 2017).

Age was determined by subtracting the date of the IFLS-5 study from the respondent's date of birth, and then the answer is categorized into 2 age groups which are <40 years and >40 years. Sex was classified into two groups which are female and male. Education was assessed with the question, "What is your highest level of education?" and the answers are categorized into three groups, which are low, medium, and high levels of education. Work was assessed with the question "what do fieldwork in your workplace?" and the answers are categorized into two groups which are indoor and outdoor workers. Place of residence was classified into two groups: rural and urban areas. Tobacco use was assessed using four questions, covering whether the respondents had ever had a habit of chewing tobacco, smoking tobacco, or smoking cigarettes/cigars (yes/no), at what age they had stopped smoking altogether (... .years/do not know), at what age they had first started smoking regularly (... years/do not know), and whether they still smoke when they ill (yes / no).

Figure 1. Sample selection flow of Indonesia Family Life Survey (IFLS-5)

The dependent variable was COPD status, and the independent variables were age, sex, education, occupation, smoking habits, age of quitting smoking, age of first smoking, smoking when ill, residence condition, and BMI. Descriptive statistics were used to describe the variables of the study population, and the chi-square test was used to calculate the difference in the proportion of each variable. Logistic regression analysis was used to test for significant determinants of the incidence of COPD. This study also examine whether there were linear relationships with exposure categories in each variable in the assessment of the prevalence of COPD. Cross-sectional analysis was used to correct the sample reduction between the years
1993 and 2014 included excess sampling in urban areas and outside Java. Cross-sectional matching was carried out with populations in 13 provinces in Indonesia in 2014 to represent the IFLS sample in that population. The confidence interval of 95% and the p-value were selected based on the appropriate study design. Stata version 14.2 software (Stata Corporation, college station, TX, USA) was used for all analyses. The IFLS carried out in 13 provinces was approved by the ethical review board of RAND and the University of Gajah Mada in Indonesia to represent an IFLS sample adapted to population in the Indonesian provinces in 2014. The current research was based on publicly available data. The use of the dataset analyzed in this study was approved by the Health Research Ethics Committee of the Faculty of Dentistry of Universitas Airlangga (#483/HRECC. FODM/VII/2019).

RESULTS

This research was conducted on a sample of 34,231 people across all age groups. The results show that 1.81% of the respondents suffered from COPD. The data obtained show that the majority of respondents surveyed (59.43%) were in the <40 years age group, were female (52.32%), had a low level of education (54.22%), and had indoor jobs (74.75%). A total of 36.74% respondents answered yes regarding having smoking habits, with 31.85% stating that they were still smoking. Those who had quit smoking at an age <40 years accounted for 2.50%, while 33.79% had begun to smoke at an age <40 years, and 7.27% still smoke when they ill. A majority of the respondents resided in urban areas (59.23%). BMI levels indicated obesity in 29.32% of respondents (Table 1).

Table 1 shows that the majority of the patients with COPD were in the age group >40 years (55.02%), were male (53.40%), were highly educated (16.02%), had an indoor job (83.59%), never had smoking habit (58.58%), resided in urban areas (67.31%), and had an overweight BMI measurement (24.92%). Of those respondents who had COPD and had a history of smoking habits, the majority quit at an age >40 years (7.77%), had first begun smoking at an age of <40 years (38.03%), and had not smoking when they were ill (27.51%).

Table 1 shows the risk factors indicated for the development of COPD, including age >40 years (p = 0.02; PR = 1.20; 95% CI = 1.02–1.41), male (p = 0.01; PR = 1.26; 95% CI = 1.07–1.49), outdoor work (p = 0.01; PR = 0.58; 95% CI = 0.46–0.72), smoking (p = 0.01; PR = 1.22; 95% CI = 1.03–1.44), age of starting to smoke (p = 0.02; PR = 1.22; 95% CI = 1.03–1.44), residence in urban areas (p = 0.01; PR = 1.43; 95% CI = 1.20–1.70), underweight BMI (p = 0.01; PR = 2.17; 95% CI = 1.76–2.66), and obese (p = 0.01; PR = 0.68; 95% CI = 0.54–0.85).

DISCUSSION

There was a significant difference between age groups in terms of the incidence of COPD. Respondents in the age group >40 years were 1.20 times more likely to suffer from COPD compared with those aged <40 years. Age is thus a risk factor associated with COPD. This is related to pulmonary function: as an individual ages, the likelihood of a decline in their lung function capacity increases. The respiratory system declines in those aged >50 years. Research in Korea has similarly stated that there is a relationship between age (>40 years) and incidence rates of COPD (Lee et al., 2015). This is also consistent with research in Bangladesh that included age among the risk factors of COPD, with a PR of 1.48 (95% CI = 1.35–1.65) (Grigsby et al., 2016).

The results of the current study also indicate a significant difference between the incidence of COPD in respondents of different genders. Previous research has also mentioned that significantly more men than women experience COPD (Lee et al., 2015), including a study in China (PR = 1.47; 95% CI = 1.09–1.90) (Yang et al., 2017). The results of the present study show that male respondents were at 1.26 times more risk of experiencing COPD than female respondents. This is because the majority of smokers in this study were male.

The results of the current study show that respondents who were outdoor workers had 0.63 times the incidence of COPD of respondents who worked indoors. This result is in line with previous studies in China which stated that outdoor workers had 1.79 times the incidence of COPD compared to indoor workers (95% CI = 2.20–6.60) (Yang et al., 2017). Outdoor jobs are also associated with outdoor air pollution; the increased air pollution can affect the respiratory tract and can lead to the development of COPD. There is previous research that states that COPD is more common among construction workers exposed to dust than among workers who are not exposed to dust (Borup, Kirkeskov, Hanskov, & Brauer, 2017).
Smoking habits in COPD

Smoking is the cause of 89% of COPD cases, with smoking when ill increasing the risk of COPD by 1.00 (95% CI: 1.00–1.44) (p = 0.02*).

| Characteristics | COPD (%) | Non-COPD (%) | Total | PR (95% CI) | p value |
|-----------------|----------|--------------|-------|-------------|---------|
| **Age (years)** |          |              |       |             |         |
| <40             | 340      | 20.002       | 20.342 | 59.43       | 1.00    | -      |
| >40             | 278      | 13.611       | 13.889 | 40.57       | 1.20    | 0.02*  |
| **Sex**         |          |              |       |             |         |
| Female          | 288      | 17.621       | 17.909 | 52.32       | 1.00    | -      |
| Male            | 330      | 15.992       | 16.322 | 47.68       | 1.26    | 0.01*  |
| **Education**   |          |              |       |             |         |
| Low             | 336      | 18.223       | 18.559 | 54.22       | 0.89    | 0.30   |
| Moderate        | 183      | 10.632       | 10.815 | 31.59       | 0.82    | 0.13   |
| High            | 99       | 16.02        | 4.758  | 14.16       | 1.00    | -      |
| **Profession**  |          |              |       |             |         |
| Indoor          | 516      | 25.072       | 25.588 | 74.75       | 1.00    | -      |
| Outdoor         | 102      | 8.541        | 8.643  | 25.25       | 0.58    | 0.01*  |
| **Smoke**       |          |              |       |             |         |
| No              | 362      | 21.292       | 21.654 | 63.26       | 1.00    | -      |
| Yes             | 256      | 12.321       | 12.577 | 36.74       | 1.22    | 0.02*  |
| **Age quit smoking** |      |              |       |             |         |
| <40 years       | 41       | 6.63         | 857    | 2.50        | 2.96    | 0.00*  |
| >40 years       | 48       | 7.77         | 781    | 2.28        | 3.85    | 0.00*  |
| Do not smoke    | 362      | 21.292       | 21.654 | 63.26       | 1.00    | -      |
| Do not know     | 167      | 10.772       | 10.939 | 31.96       | 0.91    | 0.32   |
| **First smoking age** |      |              |       |             |         |
| <40 years       | 235      | 11.330       | 11.565 | 33.79       | 1.22    | 0.02*  |
| >40 years       | 3        | 0.49         | 356    | 1.03        | 0.5     | 0.23   |
| Do not smoke    | 362      | 21.292       | 21.654 | 63.26       | 1.00    | -      |
| Do not know     | 18       | 2.91         | 656    | 1.91        | 1.66    | 0.04   |
| **Smoking when ill** |      |              |       |             |         |
| No              | 170      | 8.613        | 8.873  | 25.66       | 1.16    | 0.11   |
| Yes             | 51       | 2.438        | 2.489  | 7.27        | 1.23    | 0.17   |
| Do not smoke    | 362      | 21.292       | 21.654 | 63.26       | 1.00    | -      |
| Do not know     | 35       | 1.270        | 1.305  | 3.81        | 1.62    | 0.01   |
| **Residence**   |          |              |       |             |         |
| Rural           | 202      | 13.754       | 13.956 | 40.77       | 1.00    | -      |
| Urban           | 416      | 19.859       | 20.275 | 59.23       | 1.43    | 0.01*  |
| **BMI**         |          |              |       |             |         |
| Not measured    | 29       | 4.69         | 1.835  | 5.36        | 0.9     | 0.62   |
| Underweight     | 154      | 24.92        | 4.165  | 12.17       | 2.17    | 0.01*  |
| Normal          | 230      | 37.22        | 38.58  | 1.00        | -       |
| Overweight      | 86       | 13.92        | 4.989  | 14.57       | 0.99    | 0.93   |
| Obese           | 119      | 19.26        | 9.918  | 29.32       | 0.68    | 0.01*  |
| **Total**       | 618      | 33.613       | 34.231 | 100.00      | -       |

Our results also show that respondents who had ever smoked were at a 1.22 times higher risk of experiencing COPD compared with respondents who had never had a smoking habit. In smokers, there is a process of chronic inflammation of the airways due to the influx of inflammatory cells into the lung in response to cigarette smoke. Some of these inflammatory cells, such as macrophages, neutrophils, and CD8+T cells, have been known to play a role in the inflammatory process in the airways of patients with COPD (Yudhawati & Prasetyo, 2018). Smoking is the cause of 89%–90% of the incidence of COPD. These results are consistent with research showing a Laode Ismail chi-square test p-value of 0.03 (Ismail, Sahrudin, & Ibrahim, 2017). Smoking habits in COPD have
also been found in studies in Bangladesh (PR = 5.50; 95% CI = 4.20–7.20; p < 0.00) (Alam et al., 2015) and in China (PR = 2.09; 95% CI = 1.70–2.60) (Yang et al., 2017). Our findings also indicate that the age when an individual quits smoking has a significant influence on the development of COPD. Previous research states that the age of quitting smoking can influence the natural history of COPD with a PR value of 1.09 (95% CI = 1.06–1.08; p-value < 0.00). The severity of COPD in smokers will be worse and even have the potential to cause death in smokers who smoke at an early age and for a long time, however, COPD patients who have stopped smoking have a different risk from patients who still smoke today. The earlier the patient stops smoking, the lower the severity of COPD (Bai, Chen, Liu, Yu, & Xu, 2017).

Starting smoking at an age <40 years shows a COPD risk 2.22 times higher than that for people who started smoking aged >40. This present study is in line with previous studies which also showed similar results with PR values at smokers who started smoking aged < 40 years = 1.04 (95% CI = 1.02–1.07; p-value = 0.00. The younger a person is smoking then it will affect the maturation of pulmonary function that can lead to COPD (Bai, Chen, Liu, Yu, & Xu, 2017).

The results of the current study indicate that there is no effect of smoking while sick on the development of COPD. In a previous study involving 100 patients with COPD, 49% were smoking when they were ill (Karadogan, Onal, Sahin, & Kanbay, 2018). This contradicts with Tashkin et al (2019) findings of a significant relationship between current smoking and COPD, with p-value <0.01 (PR = 2.63; 95% CI = 1.20–2.64). If a patient smokes during their illness, it can increase the severity of COPD.

The present study’s findings show that respondents living in urban areas were 1.43 times more likely to experience COPD compared with those living in rural areas. Previous research has highlighted that there are risk factors associated with higher biomass smoke exposure in urban than rural areas, especially in Indonesian urban areas (Sana, Somda, Meda, & Bouland, 2018).

The BMI variable showed that underweight individuals had a 2.94 times higher risk of experiencing COPD than respondents with normal BMI values. This is consistent with previous research showing that there is a relationship between underweight BMI values and COPD incidence (Lin et al., 2018). For example, research conducted in Korea has shown a relationship underweight BMI values and incidence of COPD, with a PR of 3.10 (95% CI = 1.30–1.70) (Lee et al., 2015), and research in China has also shown a similar effect, with PR values of 1.09 (95%CI = 0.75–1.57) in a Han group and 2.60 (95%CI = 1.7–3.97) in a Li group (Lin et al., 2018). This study is similar to previous studies conducted in Bangladesh which showed that BMI status being in the underweight category had an effect on the incidence of COPD with a PR of 1.9 (95% CI = 1.5-2.4) (Alam, Chowdhury, Siddiquee, Ahmed, & Clemens, 2015).

**Research Limitations**

The limitation of this study is that only IFLS-5 data were used. There were many missing values in the data set, and this study only focused on the variables that influence COPD. All other information was analyzed based on the result of survey.

**CONCLUSION**

Some risk factors for the development of COPD in Indonesia include being aged >40 years, being of male gender and smoking, having begun smoking at <40 years old, and living in urban areas. Meanwhile, education, occupation, the age of quitting smoking, smoking when ill, and BMI are not direct factors causing the development of COPD.

Intervention programs that can operate at various levels of health care are indispensable in diagnosing COPD quickly and accurately. Determination of COPD diagnosis is still difficult, and late diagnosis makes COPD cases higher in Indonesia. The disease burden is also high, with COPD having become one of the contributors to 60% of deaths in Indonesia.

**CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest in this study.

**AUTHOR CONTRIBUTION**

NLF, KDA and C-YL contributed equally during the conceptualization and final approval of this study. NLF took part in the methodology, data curation, formal analysis, and writing of the original draft. KDA and C-YL took part in reviewing, editing, and revision.
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REFERENCES

Alam, D. S., Chowdhury, M. A., Siddiquee, A. T., Ahmed, S., & Clemens, J. D. (2015). Prevalence and determinants of chronic obstructive pulmonary disease (COPD) in Bangladesh. *COPD: Journal of Chronic Obstructive Pulmonary Disease, 12*(6), 658–667. https://doi.org/10.3109/15412555.2015.1041101

Bai, J. W., Chen, X. X., Liu, S., Yu, L., & Xu, J. F. (2017). Smoking cessation affects the natural history of COPD. *International Journal of COPD, 12*, 3323–3328. https://doi.org/10.2147/COPD.S150243

Borup, H., Krikkeskov, L., Hanskov, D. J. A., & Brauer, C. (2017). Systematic review: chronic obstructive pulmonary disease and construction workers. *Occupational Medicine, 67*(3), 199–204. https://doi.org/10.1093/occmed/kqx007

Global Initiative for Chronic Obstructive Lung Disease. (2018). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2018 report. Germany: Global Initiative for Chronic Obstructive Lung Disease, Inc.

Grigsby, M., Siddharthan, T., Chowdhury, M. A. H., Siddiquee, A., Rubinstein, A., Sobrino, E., ... Checkley, W. (2016). Socioeconomic status and COPD among low-and middle-income countries. *International Journal of COPD, 11*(1), 2497–2507. https://doi.org/10.2147/COPD.S111145

Ismael, L., Sahrudin, S., & Ibrahim, K. (2017). Analisis faktor risiko kejadian penyakit paru obstruktif kronik (POPK) di wilayah kerja Puskesmas Lepo-Lepo Kota Kendari tahun 2017. *Jurnal Ilmiah Mahasiswa Kesehatan Masyarakat Unsyiah, 2*(6), 1–10.

Karadogan, D., Onal, O., Sahin, D. S., & Kanbay, Y. (2018). Factors associated with current smoking in COPD patients: a cross-sectional study from the Eastern Black Sea region of Turkey. *Tobacco Induced Diseases, 16*, 1–9. https://doi.org/10.18332/tid/90665

Lamprecht, B., Soriano, J. B., Studnicka, M., Kaiser, B., Vanfleteren, L. E., Gnatiuc, L., ... Buist, S. (2015). Determinants of underdiagnosis of COPD in national and international surveys. *Chest, 148*(4), 971–985. https://doi.org/10.1378/chest.14-2535

Lee, S. J., Kim, S. W., Kong, K. A., Ryu, Y. J., Lee, J. H., & Chang, J. H. (2015). Risk factors for chronic obstructive pulmonary disease among never-smokers in Korea. *International Journal of COPD, 10*, 497–506. https://doi.org/10.2147/COPD.S77662

Lin, L., Wu, D. Y., He, P., Li, Q. N., Li, L. H., Chen, J. N., ... Ding, Y. P. (2018). The risk factors for chronic obstructive pulmonary disease in Li and Han ethnic groups in Hainan, China. *Asian Pacific Journal of Tropical Medicine, 11*(4), 305–308. https://doi.org/10.4103/1995-7645.231472

Liu, J., Zeng, X., Hong, H. G., Li, Y., & Fu, P. (2017). The association between body mass index and mortality among Asian peritoneal dialysis patients: a meta-analysis. *PLoS ONE, 12*(2), 1–14. https://doi.org/10.1371/journal.pone.0172369

López-Campos, J. L., Tan, W., & Soriano, J. B. (2015). Global burden of COPD. *Journal of the Asian Pacific Society of Respirology, 21*(1), 14–23. https://doi.org/10.1111/resp.12660

Ministry of Health RI. (2019). *Strategies for prevention and control of non-communicable diseases (PTM) in Indonesia*. Jakarta: Ministry of Health RI. Retrieved 12 December, 2019, from www.p2ptm.kemkes.go.id/profil-p2ptm/latar-belakang/startegi-pencegahan-dan-pengendalian-ptm-di-indonesia

Sana, A., Somda, S. M. A., Meda, N., & Bouland, C. (2018). Chronic obstructive pulmonary disease associated with biomass fuel use in women: a systematic review and meta-analysis. *BMJ Open Respiratory Research, 5*(1), 1–10. https://doi.org/10.1136/bmjresp-2017-000246

Soriano, J. B., Abajobir, A. A., Abate, K. H., Abers, S. F., Agrawal, A., Ahmed, M. B., ... Vos, T. (2017). Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the global burden of disease study 2015. *The Lancet Respiratory Medicine, 5*(9), 691–706. https://doi.org/10.1016/S2213-2600(17)30293-X
Strauss, J., Witoelar, F., & Sikoki, B. (2016). The fifth wave of the Indonesia family life survey: overview and field report. https://doi.org/10.7249/wr1143.1

Tashkin, D. P., Goodin, T., Bowling, A., Price, B., Ozol-Godfrey, A., Sharma, S., & Sanjar, S. (2019). Effect of smoking status on lung function, patient-reported outcomes, and safety among patients with COPD treated with indacaterol/glycopyrrolate: pooled analysis of the FLIGHT1 and FLIGHT2 studies. Respiratory Medicine, 155, 113–120. https://doi.org/10.1016/j.rmed.2019.07.019

Viniol, C., & Vogelmeier, C. F. (2018). Exacerbations of COPD. European Respiratory Review, 27(147), 1–9. https://doi.org/10.1183/16000617.0103-2017

Vogelmeier, C. F., Criner, G. J., Martinez, F. J., Anzueto, A., Barnes, P. J., Bourbeau, J., … Agustí, A. (2017). Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. American Journal of Respiratory and Critical Care Medicine, 195(5), 557–582. https://doi.org/10.1164/rccm.201701-0218PP

Yang, Y., Mao, J., Ye, Z., Li, J., Zhao, H., & Liu, Y. (2017). Risk factors of chronic obstructive pulmonary disease among adults in Chinese mainland: a systematic review and meta-analysis. Respiratory Medicine, 131, 158–165. https://doi.org/10.1016/j.rmed.2017.08.018

Yudhawati, R., & Prasetiyo, Y. D. (2018). Imunopatogenesis penyakit paru obstruktif kronik. Jurnal Respirasi, 4(1), 19–25. https://doi.org/10.20473/jr.v4-i.1.2018.19-25