Effectiveness of Fish Oil Containing Omega-3 in Improving Symptoms and Lung Function in Asthma Outpatient in Surabaya, Indonesia

Amelia Lorensia\textsuperscript{1*}, Mariana Wahyudi\textsuperscript{2}, Nadia Aisah Mayzika\textsuperscript{3}

\textsuperscript{1}Departement of Clinical-Community Pharmacy, Faculty of Pharmacy, University of Surabaya (Universitas Surabaya (UBAYA)), Surabaya
\textsuperscript{2}Departement of Purification and Molecular Biology, Faculty of Biotechnology, University of Surabaya (Universitas Surabaya (UBAYA)), Surabaya
\textsuperscript{3}Postgraduate Student of Master of Pharmacy Science, Faculty of Pharmacy, University of Surabaya (Universitas Surabaya (UBAYA)), Surabaya

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ABSTRACT
Indonesia as a potential maritime country in fish production, can be processed into fish oil containing omega-3. Based on previous libraries, omega-3 fish oils can be used to improve asthma control and improve lung function. The effects of a drug are individualized depending on genetic and environmental factors. The aim of the study was to investigate the effect of fish oil containing omega-3 on improving asthma symptoms and improving lung function. The research method used is pre-post test design, using data collection technique with asthma control test questionnaire to see clinical symptoms of asthma and measure lung function with peak flow meter. Intervention given is a fish oil product with once daily doses, then follow up every week for 4 weeks. The subject of research is adult age. Pulmonary function data and asthma symptoms will be tested for normality with shapiro-wilk test and followed by anova one way. The research was conducted in 2016-2017 in Surabaya and the data obtained 28 respondents. At the control level of asthma and total ACT score (P <0.05) it can be concluded that there was significant difference between before and after omega-3 fish oil therapy for 4 weeks. In the improvement of lung function there is a significant improvement of lung function starting from before therapy until the increase every week until the 4th week. Fish oil containing omega 3 for 4 weeks may decrease asthma symptoms in the asthma control level category and total ACT score. In addition, fish oil can also improve lung function significantly in every week.

Keywords: asthma, fish oil contains omega-3, asthma symptoms, lung function.

INTRODUCTION
Asthma is a heterogeneous disease in the form of chronic respiratory tract inflammation characterized by respiratory symptoms such as wheezing, shortness of breath, feeling depressed in the chest and cough. Despite the low level of fatality but the number of cases is quite common in the community. The World Health Organization (WHO) estimates that 100-150 million people worldwide suffer from asthma. Even this number is expected to continue to grow to reach 180,000 people every year\textsuperscript{1,2}. Adverse effects of asthma include decreased quality of life, decreased productivity, school absenteeism, increased healthcare costs, hospital care risks and even death\textsuperscript{3}. Increases in the prevalence of asthma in Asia such as Singapore, Taiwan, Japan or South Korea are also striking. The incidence of asthma has increased over fifteen years, both in developing and developed countries. In Indonesia, the prevalence of asthma is not known for certain, but it is estimated that 2-5% of Indonesia's population suffers from asthma. The Department of Health estimates that asthma is among the top 10 causes of illness and mortality in hospitals and an estimated 10% of Indonesia's 25 million people suffer from asthma. The prevalence of asthma in urban areas is generally higher than in rural areas, as urban lifestyle increases the risk of asthma. According to RISKESDAS (2013) asthma prevalence in Indonesia reached 4.5% with asthma prevalence in East Java 5.1\textsuperscript{4}.

In Indonesia, which is a maritime country, has great potential in fish production and even the government also launched GEMARIKAN in 2014, to popularize fish consumption. Fish has been known to be processed into fish oil containing high omega-3. Fish consumption can prevent asthma in adult patients. Research has shown that fish consumption at least once a month can reduce the risk of asthma\textsuperscript{6}. In the meantime, several fish oil-related studies, including omega-3s as Aprizayanti (2011)\textsuperscript{7} and Santoso et al. (2013)\textsuperscript{8}. Omega-3 has been used only as a supplement in helping the child's growth process, help lower cholesterol, heart disease. High intake of fish oil has protective effect against asthma and or allergies\textsuperscript{8}. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) consisting of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are found primarily in

\*Author for Correspondence: amelia.lorensia@gmail.com
fish oil. Epidemiological studies show that omega-3 has a protective effect against cardiovascular disease myocardial infarction or cerebral infarction, hypertension, and hyperlipidemia. In addition, omega-3 has beneficial effects on chronic inflammatory diseases including chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, and inflammation of the intestine. Atopic sensitization and allergies can also be prevented with fish intake during pregnancy.

In Indonesia has conducted several studies related to fish oil, which among others contain omega-3. Omega-3 is used as a supplement in helping the child's growth process, help lower cholesterol, heart disease, and asthma. But there has been no research related to the effect of omega-3 on the improvement of asthma in Indonesia. The anti-inflammatory effect on omega-3 is due to the content of EPA which is a competitive substrate with arachidonate so it has the potential to reduce inflammation of the respiratory tract and bronchoconstriction. This has led to a new understanding over the last 30 years that fish oil deficiency can aggravate asthma.

This study aims to determine the effect of omega-3 on the control of asthma in patients with asthma in Surabaya who

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number (n: 26)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>27,00</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>73,00</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Youth end (17-25)</td>
<td>25</td>
<td>96,15</td>
</tr>
<tr>
<td>Early adult (26-35)</td>
<td>1</td>
<td>3,85</td>
</tr>
<tr>
<td>Late adult (36-45)</td>
<td>0</td>
<td>0,00</td>
</tr>
<tr>
<td>History of Asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral agonist beta-2 short acting</td>
<td>8</td>
<td>21,05</td>
</tr>
<tr>
<td>Treatment based on</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhaled agonist beta-2 short acting</td>
<td>10</td>
<td>26,31</td>
</tr>
<tr>
<td>Global Initiative for</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen</td>
<td>1</td>
<td>2,63</td>
</tr>
<tr>
<td>Asthma (2016)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not taking any medication</td>
<td>3</td>
<td>7,89</td>
</tr>
<tr>
<td>Oral corticosteroids (used only when symptoms worsen)</td>
<td>1</td>
<td>2,63</td>
</tr>
<tr>
<td>Oral methylxanthine (used only when symptoms worsen)</td>
<td>3</td>
<td>11,53</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>Number of Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Control Based on</td>
<td></td>
</tr>
<tr>
<td>Activity Limitations</td>
<td></td>
</tr>
<tr>
<td>Too often</td>
<td>0</td>
</tr>
<tr>
<td>Often</td>
<td>2</td>
</tr>
<tr>
<td>Not too often</td>
<td>14</td>
</tr>
<tr>
<td>Never</td>
<td>9</td>
</tr>
<tr>
<td>Frequency of Shortness of</td>
<td></td>
</tr>
<tr>
<td>Breath</td>
<td></td>
</tr>
<tr>
<td>More than once a day</td>
<td>0</td>
</tr>
<tr>
<td>Once a day</td>
<td>0</td>
</tr>
<tr>
<td>3-6 times a week</td>
<td>5</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>14</td>
</tr>
<tr>
<td>Not a week at all</td>
<td>7</td>
</tr>
<tr>
<td>Symptoms Symptom Asthma</td>
<td></td>
</tr>
<tr>
<td>At Night or Morning</td>
<td></td>
</tr>
<tr>
<td>4 or more nights per week</td>
<td>2</td>
</tr>
<tr>
<td>2-3 nights per week</td>
<td>3</td>
</tr>
<tr>
<td>Once a week</td>
<td>4</td>
</tr>
<tr>
<td>Once or twice</td>
<td>6</td>
</tr>
<tr>
<td>Not at all</td>
<td>11</td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td></td>
</tr>
<tr>
<td>3 or more per day</td>
<td>1</td>
</tr>
<tr>
<td>1 or 2 times per day</td>
<td>2</td>
</tr>
<tr>
<td>2 or 3 times per week</td>
<td>4</td>
</tr>
<tr>
<td>Once a week or less</td>
<td>5</td>
</tr>
<tr>
<td>not at all</td>
<td>14</td>
</tr>
<tr>
<td>Asthma Control Based on</td>
<td></td>
</tr>
<tr>
<td>Asthma Control Level</td>
<td></td>
</tr>
<tr>
<td>Not controlled at all</td>
<td>8</td>
</tr>
<tr>
<td>Less controlled</td>
<td>6</td>
</tr>
<tr>
<td>Simply controlled</td>
<td>6</td>
</tr>
<tr>
<td>Well controlled</td>
<td>4</td>
</tr>
<tr>
<td>Full controlled</td>
<td>0</td>
</tr>
<tr>
<td>ACT Total</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled (total value of ACT: &lt;19)</td>
<td>17</td>
</tr>
<tr>
<td>Partially controlled (total value ACT: 20-24)</td>
<td>5</td>
</tr>
<tr>
<td>Full controlled (total value ACT: 25)</td>
<td>4</td>
</tr>
</tbody>
</table>
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will be given fish oil. During this treatment asthma focuses on therapy with long-term synthetic drugs, which can cause problems such as: the use of aminophylline which is a drug with a narrow range of therapy so that the risk of causing side effects 14,15,16, single use of long-acting beta-2 agonist that can aggravate Exacerbation of asthma 17, or the use of inhaled corticosteroids that may cause oropharyngeal candidiasis and even lung infections 1.

This study aims to determine the effect of fish oil containing omega-3 to improve asthma symptoms and improve lung function. Patients with a high level of education influence self evaluation so that it can affect the patient's asthma control level. This study uses research subjects with a minimum education level of high school with the hope that the level of asthma control is good, and is expected this study can also increase knowledge related to the influence of nutrition on asthma, in the role of pharmacist to support the handling of asthma by motivating patients to be obedient in treatment, Provide information, counseling, and education so that they better understand the treatment regimen provided so that patients can be more actively involved in their treatment which can improve their adherence to drug use. Treatment of asthma is a long-term treatment and adherence to medication and treatment is desirable. It is expected that good patient compliance will affect the number of drugs used less, fewer doses per day, the incidence of drug side effects is less common 3.

**METHOD**
This research uses pre-post test design method. This study used data collection techniques with Asthma Control Test questionnaire to see clinical symptoms of asthma and measure lung function with peak flow meter tool. Each sample of the study was given fish oil. Intervention given is a fish oil products circulating in Indonesia. Fish oil is given to patients with once daily doses, then follow up every week for 4 weeks. Dosage of fish oil containing

**Table 3: ACT Normality Assessment Test Group Intervention**

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>ACT0</th>
<th>ACT4</th>
<th>P value</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity Limitations</td>
<td>0,00</td>
<td>0,00</td>
<td>Distribution of data is not normal</td>
<td></td>
</tr>
<tr>
<td>Frequency of Shortness of Breath</td>
<td>0,00</td>
<td>0,00</td>
<td>Distribution of data is not normal</td>
<td></td>
</tr>
<tr>
<td>Asthma Symptoms At Night or Morning</td>
<td>0,00</td>
<td>0,00</td>
<td>Distribution of data is not normal</td>
<td></td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td>0,00</td>
<td>0,00</td>
<td>Distribution of data is not normal</td>
<td></td>
</tr>
<tr>
<td>Level of asthma control</td>
<td>0,00</td>
<td>0,00</td>
<td>Distribution of data is not normal</td>
<td></td>
</tr>
<tr>
<td>ACT Total</td>
<td>0,558</td>
<td>0,460</td>
<td>Distribution of data is normal</td>
<td></td>
</tr>
</tbody>
</table>

P> 0.05 means normal distribution; P <0.05 means the distribution is not normal

**Table 4: Changes in ACT Value as Asthma Symptoms**

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>Number of Respondents</th>
<th>Change the value of ACT0 to ACT4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Up</td>
<td>Constant</td>
</tr>
<tr>
<td>Activity Limitations</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Frequency of Shortness of Breath</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Asthma Symptoms At Night or Morning</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>Level of asthma control</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>ACT Total</td>
<td>15</td>
<td>6</td>
</tr>
</tbody>
</table>

**Table 5: ACT Differences Test Before and After Omega-3 Fish Oil Therapy.**

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>Average</th>
<th>Test the Difference</th>
<th>P value</th>
<th>Type of Test Used</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACT0</td>
<td>ACT4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activity Limitations</td>
<td>3,81</td>
<td>4,08</td>
<td>0,763</td>
<td>Friedman Test</td>
<td>There is no significant difference</td>
</tr>
<tr>
<td>Frequency of Shortness of Breath</td>
<td>4,08</td>
<td>4,23</td>
<td>0,157</td>
<td>Friedman Test</td>
<td>There is no significant difference</td>
</tr>
<tr>
<td>Asthma Symptoms At Night or Morning</td>
<td>3,81</td>
<td>4,04</td>
<td>0,317</td>
<td>Friedman Test</td>
<td>There is no significant difference</td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td>4,12</td>
<td>4,12</td>
<td>0,739</td>
<td>Friedman Test</td>
<td>There is no significant difference</td>
</tr>
<tr>
<td>Level of asthma control</td>
<td>2,08</td>
<td>3,12</td>
<td>0,00</td>
<td>Friedman Test</td>
<td>There is a significant difference</td>
</tr>
<tr>
<td>ACT Total</td>
<td>17,89</td>
<td>19,58</td>
<td>0,041</td>
<td>Anova One Way</td>
<td>There is a significant difference</td>
</tr>
</tbody>
</table>

P> 0.05, Ho accepted means there is no significant difference
P <0.05, Ho rejected means there is a significant difference
omega-3 recommended by 1 gram to 5.4 gram per day\textsuperscript{18}, then in this study selected fish oil with dose of 1.0 gram. The independent variable of this research is fish oil. While the dependent variables of this study are symptoms of asthma and lung function, with controlled variables according to inclusion and exclusion criteria. 

**Symptoms of asthma:** Symptoms of asthma were measured by using the Asthma Control Test (ACT) questionnaire. ACT is one of the specific instruments in assessing asthma control in patients with chronic asthma. Consisting of 5 questions that include activity limitation, shortness of breath, asthma symptoms at night, frequency of reliever drug use, and asthma control rate counted for 4 weeks. Each question is given a choice of 5-Likert\textsuperscript{19}. Symptoms of asthma were measured 2 times, ie, at week 0 (before intervention) and at week 4 (after intervention). Initials to use:

\[\text{ACT}_0: \text{The value of ACT at week 0, ie before getting fish oil therapy contains omega-3}\]
\[\text{ACT}_4: \text{The value of ACT at week 4, ie after getting fish oil therapy containing omega-3 for 4 weeks (one month)}\]

**Lung function:** Pulmonary function is measured from the Peak Expiratory Flow (PEF) value. PEF is the maximum ability to expel air in the lungs from the maximum inspiratory state through the mouth in liters per minute units measured by peak flow meter which is a simple and easy to apply tool\textsuperscript{1}. Pulmonary function is measured 5 times, ie once before the intervention and 3 times during intervention (after 1 week, 2 week, and 3 week intervention), and after intervention. Initials to use:

\[\text{PEF}_0: \text{PEF value at week 0, ie before getting fish oil therapy contains omega-3}\]
\[\text{PEF}_1: \text{PEF value at week 1st, after getting fish oil therapy containing omega-3 for 1 week}\]
\[\text{PEF}_2: \text{The value of PEF at week 2nd, ie after getting fish oil therapy contains omega-3 for 2 weeks}\]
\[\text{PEF}_3: \text{PEF value at week 3rd, ie after getting fish oil therapy containing omega-3 for 3 weeks}\]
\[\text{PEF}_4: \text{PEF value at week 4th, ie after getting fish oil therapy containing omega-3 for 4 weeks (one month)}\]

The population of this study were adult asthma patients (>18 years) in Surabaya. The sample (subject) of the study were adult asthma patients who were willing to engage in research and meet the requirements, namely: (1) no chronic diseases that can affect respiratory function (such as chronic respiratory illness, heart disease, chronic renal failure, etc.); (2) No smoking or consuming alcohol; and (3) not taking routine asthma medication.

Pulmonary function data and asthma symptoms will be tested the normality of data distribution by using shapiro-wilk test. If p> 0.05 then it can be concluded that normal distribution data and then proceed with one way anova to know the improvement of lung function and clinical symptoms among respondents Before and after using fish oil.

**RESULT**

The research was conducted in 2016-2017 in Surabaya. The data used in this study were obtained through the asthma control test (ACT) questionnaire given at the beginning of the first week and the end of the 4th week, peak expiratory flow (PEF) measured weekly for 5 weeks. Based on the data obtained 28 respondents, but 2 people dropped out due to allergy to fish oil and resigned because of out of town, then only 26 people who can follow the research.

**Characteristics of Respondents**

Respondents in this study were grouped by sex, age, and medical history. The number of respondents based on the characteristics of respondents includes age and gender. In the age category, the largest number is the final adolescent (17-25 years old) that is equal to 96.15% or a number of 25 people and the largest number of female respondents is 73% or 19 respondents from the total of 26 respondents. The largest number was in the respondents who used a group of agonist beta-2 short inhalation work of 26.31% in step 1 (Table 1).

**Improvement of Asthma Symptoms with Fish Oil Therapy Containing Omega-3**

Characteristics of respondents can be seen in table 2 with the depiction of each category ACT. Most of the symptoms of respondent asthma in three categories, namely: based on activity limitations, frequency of shortness of breath, frequency of asthma drug use, showed no change. But in most asthma symptoms based on asthma symptoms appearing in the evening or morning shows a decrease from the point "not at all" to "once up to two times". While asthma symptoms based on the level of control of respondents asthma increased. Based on the total of the overall ACT score, it showed improvement of most respondents with uncontrolled asthma symptoms being partially controlled (Table 2).

Normality tests across all ACT categories show all data not normally distributed, except for the total ACT values showing normal distributed data (Table 3).

The change in the value of asthma symptoms was divided into 3, ie "up" (there was an increase in ACT values after 4 weeks of fish oil), "fixed" (no change in ACT values after 4 weeks of fish oil) and "down" There was a decrease in ACT value change after being given fish oil for 4 weeks.

<table>
<thead>
<tr>
<th>Group</th>
<th>Average PEF Value (L/sec)</th>
<th>Type of Test Used</th>
<th>P value</th>
<th>Test Data Normality</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEF_0</td>
<td>217.96</td>
<td>Shapiro wilk</td>
<td>0.002</td>
<td>No normal</td>
<td></td>
</tr>
<tr>
<td>PEF_1</td>
<td>273.15</td>
<td>Shapiro wilk</td>
<td>0.131</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PEF_2</td>
<td>295.56</td>
<td>Shapiro wilk</td>
<td>0.109</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PEF_3</td>
<td>298.89</td>
<td>Shapiro wilk</td>
<td>0.209</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PEF_4</td>
<td>325.00</td>
<td>Shapiro wilk</td>
<td>0.089</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>

\(P> 0.05\) means normal distribution; \(P <0.05\) means the distribution is not normal.

\(\text{Tabel 6: Average PEF Value and Normality Test for Lung Function Data}\)
Arachidonic acid is a substrate for eicosanoid synthesis through the ALOX5 pathway. EPA and DHA suppress the production of leukotrienes with arachidonic acid that acts as an ALOX5 substrate. EPA can also suppress an allergic response to asthma by inhibiting arachidonic acid that produces leukotrienes. Leukotriene and prostaglandin E2 contribute to the formation of immunoglobulin E (IgE), an antibody that contributes to the occurrence of an allergic response. This is usually increased in patients with asthma. Although the respondents experienced an improvement in ACT scores, there were several factors that could affect the value of ACT, among others: Gender and age: In table 1, shows the largest number of samples are women than men. In boys have a greater risk in infancy and this risk decreases as they mature. While in women have a risk of staying in childhood and adulthood. The prevalence of women is higher than men, but the reason for the difference is not clear. However, at birth, men's lung size is smaller than women but as adults are larger. The risk of asthma in boys decreases as they grow older. While in women, the influence of estrogen and progesterone hormones can cause high asthma risk in women during and after puberty. Similarly, the National Center for Health Statistics (NCHS) (2011)21, which says by sex 7.2% of men and 9.7% of women that the prevalence of women is higher than men. Respondents in this study were mostly in the final adolescent category with age 17-25 years.

From table 4, it can be concluded that most improvements in asthma symptoms are seen only in the asthma level control category, whereas other categories show a fixed value. However, when viewed from the total value of ACT, showed most respondents experienced improvement (Table 4).

Test the difference of asthma symptoms based on ACT value before and after fish oil therapy in Table 5. At the control level of asthma and total ACT value (P <0.05) it can be concluded that there was significant difference between before and after fish oil therapy containing omega-3 for 4 weeks (Table 5).

**Table 7: Changes in PEF Value and Pef Value Differences Test Before and After Omega-3 Fish Oil Therapy**

<table>
<thead>
<tr>
<th>Compared groups</th>
<th>Jumlah Responden</th>
<th>Uji Perbedaan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in PEF Value (L/sec)</td>
<td>P value</td>
<td>Type of Test Used</td>
</tr>
<tr>
<td>Up</td>
<td>Constant</td>
<td>Down</td>
</tr>
<tr>
<td>PEF₀ and PEF₁</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>PEF₀ and PEF₂</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>PEF₀ and PEF₃</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>PEF₀ and PEF₄</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>PEF₁ and PEF₂</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>PEF₂ and PEF₃</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>PEF₃ and PEF₄</td>
<td>21</td>
<td>0</td>
</tr>
</tbody>
</table>

P > 0.05; Ho rejected means there is no significant difference
P < 0.05; Ho accepted means there is a significant difference.

**DISCUSSION**

**Discussion of Asthma Symptoms Improvement**

The results showed changes in ACT values that increased from uncontrolled conditions before treatment were then partially controlled after therapy. This is consistent with existing libraries that the omega-3 content of fish oil containing fatty acids has a beneficial effect on chronic inflammatory diseases including chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, and inflammatory diseases. Fish oils containing omega-3 comprising EPA and DHA suppress the production of arachidonic acid through the ALOX5 pathway. Arachidonic acid is a substrate for eicosanoid synthesis that produces an inflammatory mediator consisting of CYS-LT, prostaglandin, and thromboxane. This mediator is involved in the bronchoconstriction process and improves the respiratory tract mucus in asthma patients. EPA-enriched fish oil can inhibit the competitive production of LTC4 with arachidonic acid that acts as an ALOX5 substrate. EPA can also suppress an allergic response to asthma by inhibiting arachidonic acid that produces leukotrienes. Leukotriene and prostaglandin E2 contribute to the formation of immunoglobulin E (IgE), an antibody that contributes to the occurrence of an allergic response. This is usually increased in patients with asthma. Although the respondents experienced an improvement in ACT scores, there were several factors that could affect the value of ACT, among others: Gender and age: In table 1, shows the largest number of samples are women than men. In boys have a greater risk in infancy and this risk decreases as they mature. While in women have a risk of staying in childhood and adulthood. The prevalence of women is higher than men, but the reason for the difference is not clear. However, at birth, men's lung size is smaller than women but as adults are larger. The risk of asthma in boys decreases as they grow older. While in women, the influence of estrogen and progesterone hormones can cause high asthma risk in women during and after puberty. Similarly, the National Center for Health Statistics (NCHS) (2011) which says by sex 7.2% of men and 9.7% of women that the prevalence of women is higher than men. Respondents in this study were mostly in the final adolescent category with age 17-25 years.

**Genetic Factors:** There is a relationship between ALOX5’s genetic polymorphism and the severity of asthma, whereas ALOX5 is the code of the enzyme that produces leukotriene, which plays the role of the severity of asthma. Genetic polymorphisms of ALOX5 as well as 5-lipoxygenase-activating protein (FLAP) are associated with excessive production of leukotrienes. ALOX5 and FLAP are increased RNA messenger in peripheral blood leukocytes in asthmatics and leukotriene concentrations in...
sputum are greater in asthma patients compared with non-
asthma.13

Environmental factors (eg trigger exposure): To minimize
the influence of environmental factors in this study respon-
dents will always be required to report their activities
 during fish oil therapy, as factors such as contact with
triggers, diet, excessive physical activity, etc. may
affect the control of asthma symptoms.

Other therapies used. In the treatment history, most of
the samples used inhaled beta-2 agonist drug inhalation
group and all respondents were at step 1 treatment. Asthma
treatment is divided into controller and reliever. Controller
is a daily-used treatment in the long term to keep asthma
under clinical control through its anti-inflammatory
effects. While reliever is a treatment that is used when
necessary and quickly to reduce bronchoconstriction and
reduce the acute symptoms that accompany it. In this
study, all respondents were at step 1, which means that
none of the respondents used controller asthma medication
to maintain their daily asthma control, and all respondents
only used asthma medications when experiencing
worsening symptoms (reliever). The main choice in this
type of reliever is a short action beta-2 agonist which is
generally salbutamol with inhalation route. Inhalation
routes are preferred because they are topical, so side effects
tend to be smaller and can work directly to the target site
in the bronchioles. However, from the data of treatment
used by respondents there are some respondents who use
corticosteroids (oral or inhalation) and methylxanthine
group which is actually an asthma therapy in the controller
group.1

Discussion of Lung Function Repair
From the research results can be seen that there is an
increase in PEF value between the data before and after
the patient get therapy. This indicates a potential effect after
the respondents are given intervention in the form of fish
oil. Improvement of asthma function may be influenced by
other uncontrollable factors in research such as
psychological (stress)22,23, unpredictable weather changes
(such as cold or windy air)24,25 and daily activities.26

During the measurement of PEF values, Which can be
minimized the activity of respondents because it is done at
the same time. The factors that affect the value of PEF
but can be controlled in this study include food and drugs
consumed. Foods such as fish that contain high protein can
cause bias research results. And drugs like asthma
medication can increase the value of PEF. However, it can
be controlled from the presence of a log book given to the
patient to be filled daily containing the activities carried
out, drugs and food consumed, and adherence during the
consumption of fish oil.

Limitations of Research
Criteria for inclusion of respondents such as heart and
kidney history data were not accurately obtained. Because
when respondents say that no history of heart and kidney
is not supported by the results of checking the doctor first
by using electrocardiogram (ECG)
In this study using fish oil from a particular brand, which
does not rule out the possibility that fish oil with other
types can provide effects or not on research related asthma.

Researchers use this type of fish oil because the dose
corresponds to the desired dose of fish oil is 1.0 grams.
Therefore, respondents feel less comfortable to consume
fish oil that is considered quite large because some
respondents commented on soft capsule large enough.
Increased prevalence of asthma occurs due to genetic and
environmental factors. Asthma is a complex disease
resulting from the interaction between genetic
predisposition and environmental factors. Both of these
factors not only affect the inflammatory process but also
affect the complex and interactive phenotype.

CONCLUSION
Fish oil containing omega-3 for 4 weeks may decrease
asthma symptoms in the asthma control level category
and total ACT score. In addition, fish oil can also improve
lung function significantly in every week.

ACKNOWLEDGMENTS
Acknowledgments to DIKTI 2017 and LPPM UBAYA for
their support and support in conducting this research.

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Effectiveness of Fish Oil Containing Omega-3 in Improving Symptoms and Lung Function in Asthma Outpatient in Surabaya, Indonesia

Amelia Lorenzia1*, Mariana Wahyudi2, Nadia Aisah Mayzika3

1Department of Clinical Community Pharmacy, Faculty of Pharmacy, University of Surabaya (Universitas Surabaya (UBAYA)), Surabaya
2Department of Purification and Molecular Biology, Faculty of Biotechnology, University of Surabaya (Universitas Surabaya (UBAYA)), Surabaya
3Postgraduate Student of Master of Pharmacy Science, Faculty of Pharmacy, University of Surabaya (Universitas Surabaya (UBAYA)), Surabaya

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ABSTRACT
Indonesia as a potential maritime country, fish production, can be processed into fish oil containing omega-3. Based on previous libraries, omega-3 fish oils can be used to improve asthma control and improve lung function. The effects of a drug are individualized depending on genetic and environmental factors. The aim of the study was to investigate the effect of fish oil containing omega-3 on improving asthma symptoms and improving lung function. The research was conducted using set test design, using data collection technique with asthma control test questionnaire to see clinical symptoms of asthma and measure lung function with peak flow meter. Intervention given is a fish oil product with once daily doses, then follow up every week for 4 weeks. The subject of research is adult age. Pulmonary function data and asthma symptoms will be tested for normality with shapiro-wilk test and followed by anova one way. The research was conducted in 2016-2017 in Surabaya and the data obtained 28 respondents. At the control level of asthma and total ACT score (P <0.05) it can be concluded that there was significant difference between before and after omega-3 fish oil therapy for 4 weeks. In the improvement of lung function there is a significant improvement of lung function starting from before therapy until the increase every week until the 4th week. Fish oil containing omega 3 for 4 weeks may decrease asthma symptoms in the asthma control level category and total ACT score. In addition, fish oil can also improve lung function significantly in every week.

Keywords: asthma, fish oil contains omega-3, asthma symptoms, lung function.

INTRODUCTION
Asthma is a heterogeneous disease in the form of chronic respiratory tract inflammation characterized by respiratory symptoms such as wheezing, shortness of breath, feeling depressed in the chest and cough. Despite the low level of fatality but the number of cases is quite common in the community. The World Health Organization (WHO) estimates that 100-150 million people worldwide suffer from asthma. Even this number is expected to continue to grow to reach 180,000 people every year1,2. Adverse effects of asthma include decreased quality of life, decreased productivity, school absenteeism, increased healthcare costs, hospital care risks and even death3. Increases in the prevalence of asthma in Asia such as Singapore, Taiwan, Japan or South Korea are striking. The incidence of asthma has increased over the recent years, both in developing and developed countries. In Indonesia, the prevalence of asthma is not known for certain, but it is estimated that 2.5-5% of Indonesia's population suffers from asthma. The Department of Health estimates that asthma is among the top 10 causes of illness and mortality in hospitals and an estimated 10% of Indonesia's 25 million people suffer from asthma. The prevalence of asthma in urban areas is generally higher than in rural areas, as urban lifestyle increases the risk of asthma. According to RISKESDAS (2013) asthma prevalence in Indonesia reached 4.5% with asthma prevalence in East Java 5.1%4,5.

In Indonesia, which is a maritime country, has great potential in fish production and even the government also launched GEMARIKAN in 2014, to popularize fish consumption. Fish has been known to be processed into fish oil containing high omega-3. Fish consumption can prevent asthma in adult patients. Research has shown that fish consumption at least once a month can reduce the risk of asthma6. In the meantime, several fish oil-related studies, including omega-3s as Apriyantini (2011)7 and Santoso et al. (2013)8. Omega-3 has been used only as a supplement in helping the child's growth process, help lower cholesterol, heart disease. High intake of fish oil is protective effect against asthma and or allergies8. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) consisting of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are found primarily in

*Author for Correspondence: amelia.lorenzia@gmail.com
Table 1: Frequency Distribution of Respondent Characteristics.

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<tr>
<th>Characteristics</th>
<th>Number (n: 26)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
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<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>27.00</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>73.00</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35th end (17-25)</td>
<td>25</td>
<td>96.15</td>
</tr>
<tr>
<td>Early adult (26-35)</td>
<td>1</td>
<td>3.85</td>
</tr>
<tr>
<td>Late adult (36-45)</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>History of Asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral agonist beta-2 short acting</td>
<td>8</td>
<td>21.05</td>
</tr>
<tr>
<td>Treatment based on Inhaled agonist beta-2 short acting</td>
<td>10</td>
<td>26.31</td>
</tr>
<tr>
<td>Global Initiative for Oxygen</td>
<td>1</td>
<td>2.63</td>
</tr>
<tr>
<td>Asthma (2016)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not taking any medication</td>
<td>3</td>
<td>7.19</td>
</tr>
<tr>
<td>Oral corticosteroids (used only when symptoms worsen)</td>
<td>1</td>
<td>2.63</td>
</tr>
<tr>
<td>Oral methylxanthine (used only when symptoms worsen)</td>
<td>3</td>
<td>11.53</td>
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Table 2: Frequency Distribution Assessment of Asthma Symptoms Based on ACT.

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>Number of Respondents</th>
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<tr>
<td></td>
<td>ACT 6</td>
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<tr>
<td>Asthma Control Based on</td>
<td></td>
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<tr>
<td>Activity Limitations</td>
<td></td>
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<tr>
<td>Every now and then</td>
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<td>Too often</td>
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<td>Often</td>
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<tr>
<td>Not too often</td>
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<tr>
<td>Never</td>
<td>9</td>
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<tr>
<td>Asthma Control Based on</td>
<td></td>
</tr>
<tr>
<td>Frequency of Shortness of</td>
<td></td>
</tr>
<tr>
<td>Breath</td>
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<td>More than once a day</td>
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<tr>
<td>Once a day</td>
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<tr>
<td>3-6 times a week</td>
<td>5</td>
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<tr>
<td>Once or twice a week</td>
<td>14</td>
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<td>11 times a week</td>
<td>7</td>
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<tr>
<td>Asthma Control Based on</td>
<td></td>
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<tr>
<td>Symptoms Symptom Asthma</td>
<td></td>
</tr>
<tr>
<td>At Night or Morning</td>
<td></td>
</tr>
<tr>
<td>4 or more nights per week</td>
<td>2</td>
</tr>
<tr>
<td>2-3 nights per week</td>
<td>3</td>
</tr>
<tr>
<td>Once a week</td>
<td>4</td>
</tr>
<tr>
<td>Once or twice</td>
<td>6</td>
</tr>
<tr>
<td>0 at all</td>
<td>11</td>
</tr>
<tr>
<td>Asthma Control Based on</td>
<td></td>
</tr>
<tr>
<td>Frequency of Asthma Drug</td>
<td></td>
</tr>
<tr>
<td>Use</td>
<td></td>
</tr>
<tr>
<td>3 or more per day</td>
<td>1</td>
</tr>
<tr>
<td>1 or 2 times per day</td>
<td>2</td>
</tr>
<tr>
<td>2 or 3 times per week</td>
<td>4</td>
</tr>
<tr>
<td>Once a week or less</td>
<td>5</td>
</tr>
<tr>
<td>Not at all</td>
<td>14</td>
</tr>
<tr>
<td>Asthma Control Based on</td>
<td></td>
</tr>
<tr>
<td>Asthma Control Level</td>
<td></td>
</tr>
<tr>
<td>Not controlled at all</td>
<td>8</td>
</tr>
<tr>
<td>Less controlled</td>
<td>6</td>
</tr>
<tr>
<td>Simply controlled</td>
<td>6</td>
</tr>
<tr>
<td>Well controlled</td>
<td>4</td>
</tr>
<tr>
<td>Full controlled</td>
<td>0</td>
</tr>
<tr>
<td>ACT Total</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled (total value of ACT: &lt;19)</td>
<td>17</td>
</tr>
<tr>
<td>Partially controlled (total value ACT: 20-24)</td>
<td>5</td>
</tr>
<tr>
<td>Full controlled (total value ACT: 25)</td>
<td>4</td>
</tr>
</tbody>
</table>

Fish oil. Epidemiological studies show that omega-3 has a protective effect against cardiovascular disease myocardial infarction or cerebral infarction, hypotension, and hyperlipidemia. In addition, omega-3 has beneficial effects on chronic inflammatory diseases including chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, and inflammation of the intestine. Atopic sensitization and allergies can also be prevented with fish intake during pregnancy. But there has been no research related to the effect of omega-3 on the improvement of asthma in Indonesia. The anti-inflammatory effect on omega-3 is due to the content of EPA which is a competitive substrate with arachidonic acid, so it has the potential to reduce inflammation of the respiratory tract and bronchoconstriction. This has led to a new understanding and for the past 30 years that fish oil deficiency can be a cause of asthma. This study aims to determine the effect of omega-3 on the control of asthma in patients with asthma in Surabaya who...
Table 3: ACT Normality Assessment Test Group Intervention

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>ACT&lt;sub&gt;0&lt;/sub&gt;</th>
<th>ACT&lt;sub&gt;4&lt;/sub&gt;</th>
<th>P value</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity Limitations</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td>Distribution of data is not normal</td>
</tr>
<tr>
<td>Frequency of Shortness of Breath</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td>Distribution of data is not normal</td>
</tr>
<tr>
<td>Asthma Symptoms At Night or Morning</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td>Distribution of data is not normal</td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td>Distribution of data is not normal</td>
</tr>
<tr>
<td>Level of asthma control</td>
<td>0.001</td>
<td>0.044</td>
<td></td>
<td>Distribution of data is normal</td>
</tr>
<tr>
<td>ACT Total</td>
<td>0.558</td>
<td>0.460</td>
<td></td>
<td>Distribution of data is normal</td>
</tr>
</tbody>
</table>

P < 0.05 means normal distribution; P < 0.05 means the distribution is not normal

Table 4: Changes in ACT Value as Asthma Symptoms

<table>
<thead>
<tr>
<th>Asthma Assessment Category</th>
<th>Number of Respondents</th>
<th>Change the value of ACT&lt;sub&gt;0&lt;/sub&gt; to ACT&lt;sub&gt;4&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Up</td>
<td>Constant</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Activity Limitations</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Frequency of Shortness of Breath</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Asthma Symptoms At Night or Morning</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>Level of asthma control</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>ACT Total</td>
<td>15</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 5: ACT Differences Test Before and After Omega-3 Fish Oil Therapy

<table>
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<tr>
<th>Asthma Assessment Category</th>
<th>Average</th>
<th>Test the Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ACT&lt;sub&gt;0&lt;/sub&gt;</td>
<td>ACT&lt;sub&gt;4&lt;/sub&gt;</td>
</tr>
<tr>
<td>Activity Limitations</td>
<td>3.81</td>
<td>4.08</td>
</tr>
<tr>
<td>Frequency of Shortness of Breath</td>
<td>4.08</td>
<td>4.23</td>
</tr>
<tr>
<td>Asthma Symptoms At Night or Morning</td>
<td>3.81</td>
<td>4.04</td>
</tr>
<tr>
<td>Frequency of Asthma Drug Use</td>
<td>4.12</td>
<td>4.12</td>
</tr>
<tr>
<td>Level of asthma control</td>
<td>2.08</td>
<td>3.12</td>
</tr>
<tr>
<td>ACT Total</td>
<td>17.89</td>
<td>19.58</td>
</tr>
</tbody>
</table>

P < 0.05, Ho accepted means there is no significant difference
P < 0.05, Ho rejected means there is a significant difference

will be given fish oil. During this treatment asthma focuses on therapy with long-term synthetic drugs, which can cause problems such as: the use of aminophylline which is a drug with a narrow range of therapy so that the risk of causing side effects[11,12]; single use of long-acting beta-2 agonist that can aggravate Exacerbation of asthma[13]; or the use of inhaled corticosteroids that may cause oropharyngeal candidiasis and even lung infections[14]. This study aims to determine the effect of fish oil containing omega-3 to improve asthma symptoms and improve lung function. Patients with a high level of education influence self evaluation so that it can affect the patient's asthma control level. This study uses research subjects with a minimum education level of high school with the hope that the level of asthma control is good, and is expected this study can also increase knowledge related to the influence of nutrition on asthma, in the role of pharmacist to support the handling of asthma by motivating patients to be obedient in treatment, Provide information, counseling, and education so that they better understand the treatment regimen provided so that patients can be more actively involved in their treatment which can improve their adherence to drug use. Treatment of asthma is a long-term treatment and adherence to medication and treatment is desirable. It is expected that good patient compliance will affect the number of drugs used less, fewer doses per day, the incidence of drug side effects is less common.

METHOD

This research uses pre-post test design method. This study used data collection techniques with Asthma Control Test questionnaire to see clinical symptoms of asthma and measure lung function with peak flow meter tool. Each sample of the study was given fish oil. Intervention given is a fish oil products circulating in Indonesia. Fish oil is given to patients with once daily doses, then follow up every week for 4 weeks. Dosage of fish oil containing...
omega-3 recommended by 1 gram to 5.4 gram per day18, then this study selected fish oil with dose of 1.0 gram. The independent variable of this research is fish oil. While the dependent variables of this study are symptoms of asthma and lung function, with controlled variables according to inclusion and exclusion criteria.

**Symptoms of asthma**: Symptoms of asthma were measured by using the Asthma Control Test (ACT) questionnaire. ACT is 11 of the specific instruments in assessing asthma control in patients with chronic asthma. Completing of 5 questions that include activity limitation, shortness of breath, asthma symptoms at night, frequency of reliever drug use, and asthma control rate counted for 4 weeks. Each question is given a choice of 5- Likert 119. Symptoms of asthma were measured 2 times, ie, at week 0 (before intervention) and at week 4 (after intervention). Initiates to use:

**ACT**: The value of ACT at week 0, ie before getting fish oil therapy contains omega-3

**ACT**: The value of ACT at week 4, ie after getting fish oil therapy containing omega-3 for 4 weeks (one month)

**Lung function**: Pulmonary function is measured on the Peak Expiratory Flow (PEF) value. PEF is the maximum ability to expel air in the lungs from the maximum inspiratory state through the mouth in liters per minute units measured by peak flow meter which is a simple and easy to apply tool. Pulmonary function is measured 5 times, ie once before the intervention and 3 times during intervention (after 1 week, 2 week, and 3 week intervention), and after intervention. Initiates to use:

**PEF**: PEF value at week 0, ie before getting fish oil therapy contains omega-3

**PEF**: PEF value at week 1st, after getting fish oil therapy containing omega-3 for 1 week

**PEF**: The value of PEF at week 2nd, ie after getting fish oil therapy contains omega-3 for 2 weeks

**PEF**: PEF value at week 3rd, ie after getting fish oil therapy containing omega-3 for 3 weeks

**PEF**: PEF value at week 4th, ie after getting fish oil therapy containing omega-3 for 4 weeks (one month)

The population of this study were adult asthma patients (> 18 years) in Surabaya. The sample (subject) of the study were adult asthma patients who were willing to engage in research and meet the requirements, namely: (1) no chronic diseases that can affect respiratory function (such as chronic respiratory illness, heart disease, chronic renal failure, etc.); (2) No smoking or consuming alcohol; and (3) not taking routine asthma medication.

Pulmonary function data and asthma symptoms will be tested the normality of data distribution by using shapiro-wilk test. If p > 0.05 then it can be concluded that normal distribution data and then proceed with one way anova to know the improvement of lung function and clinical symptoms among respondents before and after using fish oil.

**RESULT**

The research was conducted in 2016-2017 in Surabaya. The data used in this study were obtained through the asthma control test (ACT) questionnaire given at the beginning of the first week and the end of the 4th week, peak expiratory flow (PEF) measured weekly for 5 weeks. Based on the data obtained 28 respondents, but 2 people dropped out due to allergy to fish oil and resigned because out of town, then only 26 people can follow the research.

**Characteristics of Respondents**

Respondents in this study were grouped by sex, age, and medical history. The number of respondents based on the characteristics of respondents includes age and gender. In the age category, the largest number is the final adolescent (17-25 years old) that is equal to 96.15% or a number of 25 people and the largest number of female respondents is 73% or 19 respondents from the total of 26 respondents. The largest number was in the respondents who used a group of agonist beta-2 short inhalation work of 26.31% in step 1 (Table 1).

**Improvement of Asthma Symptoms with Fish Oil Therapy Containing Omega-3**

Characteristics of respondents can be seen in table 2 with the depiction of each category ACT. Most of the symptoms of respondent asthma in three categories, namely: based on activity limitations, frequency of shortness of breath, frequency of asthma drug use, showed no change. But in most asthma symptoms based on asthma symptoms appearing in the evening or morning shows a decrease from the point "not at all" to "once up to two times". While asthma symptoms based on the level of control of respondents asthma increased. Based on the total of the overall ACT score, it showed improvement of most respondents with uncontrolled asthma symptoms being partially controlled (Table 2).

Normality tests across all ACT categories show all data not normally distributed, except for the total ACT values showing normal distributed data (Table 3).

The change in the value of asthma symptoms divided into 3, ie "up" (there was an increase in ACT values), "fixed" (no change in ACT values after 4 weeks of fish oil), and "down" (there was a decrease in ACT value change after being given fish oil for 4 weeks).
Table 7: Changes in PEF Value and Pef Value Differences Test Before and After Omega-3 Fish Oil Therapy.

<table>
<thead>
<tr>
<th>Compared groups</th>
<th>Jumlah Responden</th>
<th>Uji Perbedaan</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Changes in PEF Value (L/sec)</td>
<td>P value</td>
<td>Type of Test Used</td>
</tr>
<tr>
<td></td>
<td>Up</td>
<td>Constant</td>
<td>Down</td>
</tr>
<tr>
<td>PEF0 and PEF1</td>
<td>20</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>PEF0 and PEF2</td>
<td>21</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>PEF0 and PEF3</td>
<td>20</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>PEF0 and PEF4</td>
<td>24</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>PEF1 and PEF2</td>
<td>20</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>PEF2 and PEF3</td>
<td>16</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>PEF3 and PEF4</td>
<td>21</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>

0.05: Ho rejected means there is no significant difference
P <0.05: Ho accepted means there is a significant difference

From table 4, it can be concluded that most improvements in asthma symptoms are seen only in the asthma level control category, whereas other categories show a fixed value. However, when viewed from the total value of ACT, showed most respondents experienced improvement (Table 4).

Test the difference of asthma symptoms based on ACT value before and after fish oil therapy in table 5. At the control level of asthma and total ACT value (P <0.05) it can be concluded that there was significant difference between before and after fish oil therapy containing omega-3 for 4 weeks (Table 5).

Improvement of Lung Function with Omega-3 Fish Oil Therapy

The Difference Test describes the average PEF score obtained once a week after the respondents get a fish oil intervention for 4 weeks. The largest number was in the intervention group at week 4 with an average of 325.00 (Table 6).

Based on the normality test from table 6 indicating that there is data showing abnormal distribution (PEF0 data), the difference test using Friedman Test (Table 7). Based on the difference test, it was concluded that there was a significant improvement on every week (Table 7).

DISCUSSION
Discussion of Asthma Symptoms Improvement

The results showed changes in ACT values that increased from uncontrolled conditions before treatment were then partially controlled after therapy. This is consistent with existing hypotheses that the omega-3 content of fish oils containing fatty acids has a beneficial effect on chronic inflammatory diseases including chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, and inflammatory disorders. Fish oils containing omega 3 comprising EPA and DHA suppress the production of arachidonic acid through the ALOX5 pathway. Arachidonic acid is a substrate for eicosanoid synthesis that produces an inflammatory mediator consisting of CYS-LT, prostaglandin, and thromboxane. This mediator is involved in the bronchoconstriction process and improves the respiratory tract dilatation in asthma patients. EPA-enriched fish oil can inhibit the competitive production of LTC4 with arachidonic acid that acts as an ALOX5 substrate. EPA can also suppress an allergic response to asthma by inhibiting arachidonic acid that produces leukotrienes. Leukotriene and prostaglandin E2 contribute to the formation of immunoglobulin E (IgE), an antibody that contributes to the occurrence of an allergic response. This is usually increased in patients with asthma. Although the respondents experienced an improvement in ACT scores, there were several factors that could affect the value of ACT, among others: Gender and age: In table 1, shows the largest number of samples are women than men. In boys a greater risk in infancy and this risk decreases as they mature while in women have a risk of staying in childhood and adulthood. The prevalence of women is higher than men, but the reason for the difference is not clear. However, at birth, men's lung size is smaller than women but as adults are larger. The risk of asthma in boys decreases as they grow older. While in women, the influence of estrogen and progesterone hormones can cause high asthma risk in women during and after puberty. Similarly, the National Center for Health Statistics (NCHS) (2011), which says by sex 7.2% of men and 9.7% of women that the prevalence of women is higher than men. Respondents in this study were mostly in the final adolescent category with age 17-25 years.

Genetic Factors: There is a relationship between ALOX5's genetic polymorphism and the severity of asthma, whereas ALOX5 is the code of the enzyme that produces leukotriene, which plays the role of the severity of asthma. Genetic polymorphisms of ALOX5 as well as 5-lipoxygenase-activating protein (FLAP) are associated with excessive production of leukotrienes. ALOX5 and FLAP are increased RNA messenger in peripheral blood leukocytes in asthmatics and leukotriene concentrations in
sputum are greater in asthma patients compared with non-
asthma.

Environmental factors (e.g., trigger exposure): To minimize
the influence of environmental factors in this study
respondents will always be required to report their
activities during fish oil therapy, as factors such as contact
with triggers, diet, excessive physical activity, etc. may
affect the control of asthma symptoms.

Other therapies used. In the treatment history, most of
the samples used included beta-2 agonist drug inhalation
group and all respondents were at step I treatment. Asthma
treatment is divided into controller and reliever. Controller
is a daily-used treatment in the long term to keep asthma
under clinical control through its anti-inflammatory
effects. While reliever is a treatment that is used when
necessary and quickly to reduce bronchoconstriction and
reduce the acute symptoms that accompany it. In this
study, all respondents were at step 1, which means that
none of the respondents used controller asthma medication
to maintain their daily asthma control, and all respondents
only used asthma medications when experiencing
worsening symptoms (reliever). The main choice in this
type of reliever is a short-acting beta-2 agonist which is
generally salbutamol with inhalation route. Inhalation
routes are preferred because they are topical, so side effects
tend to be smaller and can work directly to the target site
in the bronchioles. However, from the data of treatment
used by respondents there are some respondents who use
corticosteroids (oral or inhalation) and methylxanthine
group which is actually an asthma therapy in the controller
group.

Discussion of Lung Function Repair

From the research results can be seen that there is an
increase in PEF value between the data before and after
the patient get therapy. This indicates a potential effect after
the respondents are given intervention in the form of fish
oil. Improvement of asthma function may be influenced by
other uncontrollable factors in research such as
psychological (stress), unpredictable weather changes
(such as cold or windy air), and daily activities.

During the measurement of PEF values, which can be
minimized the activity of respondents because it is done at
the same time. The factors that affect the value of PEF but
can be controlled in this study include food and drugs
consumed. Foods such as fish that contain high protein can
cause bias research results. And drugs like asthma
medication can increase the value of PEF. However, it can
be controlled from the presence of a log book given to the
patient to be filled daily containing the activities carried
out, drugs and food consumed, and adherence during the
consumption of fish oil.

Criteria for inclusion of respondents such as heart and
kidney history data were not accurately obtained. Because
when respondents say that no history of heart and kidney
is not supported by the results of checking the doctor first
by using electrocardiogram (ECG).

In this study using fish oil from a particular brand, which
does not rule out the possibility that fish oil with other
types can provide effects or not on research related asthma.

Researchers use this type of fish oil because the dose
Corresponds to the desired dose of fish oil is 1.0 grams.
Therefore, respondents feel less comfortable to consume
fish oil that is considered quite large because some
respondents commented on soft capsule large enough.

Increased prevalence of asthma occurs due to genetic
and environmental factors. Asthma is a complex disease
resulting from the interaction between genetic
predisposition and environmental factors. Both of these
factors not only affect the inflammatory process but also
affect the complex and interactive phenotype.
The number of samples in this study were 26 people.
Researchers have difficulty in finding a large number of
to get valid results. Researchers should be able to
work with health centers or other health agencies so that
the number of samples can be reproduced.

Researchers cannot control racial factors that can affect
genetic outcomes. Therefore it is necessary to do further
research related to genetic influence (polymorphism of
ALOX5) on therapeutic effect of fish oil containing
omega-3.

CONCLUSION

Fish oil containing omega-3 for 4 weeks may decrease
asthma symptoms in the asthma control level category and
total ACT score. In addition, fish oil can also improve lung
function significantly in each week.

ACKNOWLEDGMENTS

Acknowledgments to DIKTI 2017 and LPPM UBAYA for
their support and support in conducting this research.

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dan Isolat Antihistamin N Terhadap Kadar Lemak dan

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